



Associations between methamphetamine use, psychiatric comorbidities and treatment outcome in two inpatient rehabilitation centers

Proebstl Lisa^a, Kamp Felicia^{a,*}, Hager Laura^a, Krause Daniela^a, Riebschläger Marlies^b, Neumann Stefanie^b, Schacht Jablonowsky Maik^b, Schreiber Anne^c, Straif Maximilian^c, Manz Kirsi^d, Soyka Michael^{a,e}, Koller Gabi^a

^a Department of Psychiatry and Psychotherapy University Hospital Munich, LMU Munich, Nussbaumstraße 7, Munich 80336, Germany

^b MEDIAN Clinic Mecklenburg, Dorfstraße 3, Vitense 19217, Germany

^c District Hospital Hochstadt, Hauptstraße 13, Hochstadt am Main 96272, Germany

^d Institute for Medical Information Processing, Biometry and Epidemiology, Ludwig-Maximilians-University, Marchioninstraße 15, Munich 81377, Germany

^e Medical Parc Chiemseeblick, Rathausstraße 8, Bernau am Chiemsee 83233, Germany

ARTICLE INFO

Keywords:

Stimulants
Dropout
Addiction
Depression
Substance use

ABSTRACT

The use of methamphetamine is spreading globally and provokes the need for effective treatment options. Previous research showed increased psychiatric comorbidities in methamphetamine users, but its impact on treatment success is still unclear. This study investigates data from two German addiction rehabilitation centers including 108 methamphetamine using individuals. The participants were tested and interviewed at the beginning of the addiction treatment program and at the end of treatment after about six months. In total, 95% of the participants had at least another psychiatric diagnosis. At admission, substance related comorbid diagnoses (meaning abuse or addiction of other substances than methamphetamine) showed a significant effect on treatment dropout. Within the substance related diagnoses, the majority of participants (62%) suffered from cannabinoid dependency. Non-substance related comorbidities and the total number of comorbid diagnoses did not have an impact on treatment outcome. The most frequent non substance specific diagnosis at admission was a depressive disorder (15%). Diagnoses patients had at discharge did not show any effects on the treatment completion. Comparing diagnoses at admission and discharge revealed slight differences, which may rise from a better assessment at discharge due to the fact that clinicians got to know the patients better during the therapeutic process.

1. Introduction

Over the past 10 years, the use of methamphetamine (MA) and the number of related deaths have increased greatly (Bose et al., 2016). In 2010, there were about 7 million people using MA (European Monitoring Centre for Drugs and Drug Addiction, 2010), while in 2017, there were about 17.5 million people consuming the substance (European Monitoring Centre for Drugs and Drug Addiction, 2017). In the European Union, the lifetime use is 1.0% (European Monitoring Centre for Drugs and Drug Addiction, 2017), while it is even higher in other regions. The highest prevalence of the use of amphetamines (including MA) is seen in North America with 2.0%, followed by Oceania with 1.3% among the population aged 15 to 64 years (United Nations Office on Drugs and Crime, 2018).

Besides the negative health consequences of substance use itself,

there is evidence for psychomotor impairment (Volkow et al., 2001) and higher psychiatric comorbidity rates in substance users compared with the general population (McGovern et al., 2006; Lai et al., 2015). This could occur because the consumption of MA has strong effects on the central nervous system, mainly it causes a downregulation of the dopamine system because of an increased neurotransmitter release (Prakash et al., 2017; Proebstl et al., 2019). Additionally research found that MA also affects inflammatory pathways in the brain, which is also associated with the development of depression and psychosis (Papageorgiou et al., 2019). Concerning MA use, Zweben et al. (2004) investigated comorbidity rates within an outpatient MA treatment project in a large study sample and found that 68% of women and 50% of men reported a history of feeling depressed, with a mean Beck Depression Inventory (BDI) score of 15.48. Chen et al. (2003) investigated a group of MA users (recruited from treatment and a detention center)

* Corresponding author.

E-mail address: Felicia.Kamp@med.uni-muenchen.de (K. Felicia).

<https://doi.org/10.1016/j.psychres.2019.112505>

Received 8 May 2019; Received in revised form 31 July 2019; Accepted 31 July 2019

Available online 01 August 2019

0165-1781/ © 2019 Elsevier B.V. All rights reserved.

with and without psychosis and found a depression rate ranging from 3.8% to 4.6% for the nonpsychosis group, and about one-fifth of the study population showed comorbid alcohol use. A review by Darke et al. (2008) reported that the psychopathological harms demonstrated by amphetamine users and MA users were mainly substance-induced psychosis, mood and anxiety disorders, and cognitive deficits. Salo et al. (2011) also examined the prevalence of psychiatric comorbidities within a population of MA users. They found that one-third of the population reported lifetime depression symptoms that were not substance induced as well as a high number of participants with anxiety disorders (26.5%). However, 28.6% of their participants also had a psychotic disorder, which was mainly substance induced.

When looking at the effects of the association between substance use and psychiatric symptoms, it was shown that psychiatric comorbidities are a main reason for ongoing substance abuse or relapse (Sinha, 2001), which is again one main reason for treatment termination. Previous research about comorbidity rates in MA users often neglected associated treatment outcomes, which is why this paper aims to investigate current comorbidity rates from participants of an inpatient MA treatment program and to evaluate its influence on treatment dropout.

2. Method

2.1. Study design

All participants were recruited in rehabilitation programs for MA users within two German addiction treatment centers, the Institution Clinic of Hochstadt (HS) and MEDIAN Clinic in Mecklenburg (MB). Data for this study were collected within a project funded by the German federal ministry of health (Soyka et al., 2017) at two measuring times: T0 (baseline, after withdrawal, within the first 2 weeks of rehabilitation treatment) and T1 (end of rehabilitation treatment, approximately 24 weeks). The Ethic Commission of the University Hospital Munich approved the study protocol, and all participants signed an informed consent.

2.2. Participants

All participants were recruited as formerly MA-consuming inpatients in one of the two treatment centers after withdrawal. All participants were abstinent from alcohol, MA and other illegal substances for the time of their treatment and at all test times. Inclusion criteria were a signed informed consent, inpatient treatment in one of the above stated centers because of previous MA consumption (diagnosed ICD-10 diagnosis F15.2 within the admission process in the rehabilitation centers, meaning mental and behavioral disorders due to use of MA), and a minimum age of 18 years. Subjects were excluded if they had any florid psychotic disorders, if they were not able to read or understand the tests properly, or if they were intoxicated by any substance (urine tests were performed). All participants were paid €50 for their participation, €15 after the completion of the first two measurements. Continuous urine samples and breath alcohol tests were routinely collected in both centers to obtain an objective measurement of abstinence or substance use during the treatment.

2.3. Instruments

Participants answered several interviews and questionnaires. All instruments were used in their German versions. The Wender Utah Rating Scale (WURS-k) (Retz-Junginger et al., 2002) was used to assess symptoms of hyperkinetic disorders at the baseline measurement. Also at T0, specially trained study personal assessed the semistructured clinical interview for current and especially lifetime information about DSM-IV Axis I disorders (SCID, German version by Wittchen et al. (1997)) to determine major mental disorders. In addition to the SCID results, all ICD diagnoses out of medical reports such as

admission and discharge letters were extracted. Interviewers were blind to all clinical diagnoses of the participants, except for their history of MA use. The BDI-II (Hautzinger et al., 2009), as an instrument for depression, was filled out at T0 by almost all participants and at T1 mainly by the completers. To gain as much information as possible on other diagnoses as the main reason for MA consumption, we also recorded all diagnoses rated at treatment beginning and end by the clinicians in the respective centers. The clinicians obtained these ratings by their own clinical impression and at the time of the admission by previous medical reports.

2.4. Statistical analyses

Statistical analyses were performed with IBM SPSS Statistics 24. First univariate statistics, such as frequencies, means, and standard deviations (sd) were calculated. In the second step, univariate as well as multivariate statistics such as logistic regression models were calculated to determine the impact of different variables on treatment outcome. *T*-tests were used for assessing differences in means between two normally distributed continuous variables, and for comparison of two categorical variables, χ^2 tests were performed. The significance level was set at $p = 0.05$.

3. Results

3.1. Participants

In total, 108 participants were recruited within the two treatment centers and participated in the baseline measurement (T0). Eighty-six subjects (77%) were male, and 22 (23%) were female. The mean age of the study population was 31.67 years (sd = 7.70). From this original sample, 64 patients (59%) completed the treatment as scheduled, while 44 patients (41%) dropped out early. In total, 56 (87%) of the 64 completers and 1 (2%) of the 44 early dropouts participated the T1 testing. There was no significant difference in treatment drop out between both centers ($p = 0.35$, $BF_{01} = 1.87$). When comparing the number of comorbid diagnoses in the two centers, participants from HS had more diagnoses at admission ($p < 0.01$) but not at discharge ($p = 0.13$, $BF_{01} = 2.31$).

3.2. Lifetime and current diagnoses analyzed by the SCID and WURS-K

In total, 93 of 108 participants were interviewed with the SCID, since 15 subjects refused to take part in the interview. Thirteen of the 98 participants (14%) were diagnosed as currently suffering from major depression, 11 participants (11.8%) had a current anxiety disorder, another 11 subjects showed a current or lifetime post-traumatic stress disorder (PTSD), 5 individuals (5.4%) currently suffered from obsessive compulsive disorder (OCD), 2 subjects (2.2%) showed a current somatoform disorder, and another 2 participants had a current eating disorder. See Fig. 1 for all SCID diagnoses, including lifetime diagnoses.

There was a significant difference ($t(91) = 2.56$, $p = 0.03$) in the means of additional addiction SCID diagnoses between those with a current OCD diagnosis (mean = 3.20, sd = 0.84) and those without an OCD diagnosis (mean = 2.05, sd = 1.12) as well as in the total number of diagnoses ($t(5.65) = 4.02$, $p < 0.01$) in participants with current OCD (mean = 4.00, sd = 0.77) and without OCD (mean = 2.61, sd = 1.29). No significant differences were found in the number of addiction diagnoses at discharge in participants with or without the following current SCID diagnoses: depression ($p = 0.48$), anxiety ($p = 0.61$), PTSD ($p = 0.51$), somatoform disorders ($p = 0.26$), and eating disorders ($p = 0.26$).

Among patients with attention-deficit hyperactivity disorder (ADHD; WURS-k, $n = 76$, mean = 28.61, sd = 18.61) and those with a critical WURS-k score > 29 ($n = 33$, 47%), there was no significant difference between the two centers in the total WURS-k score ($p = 0.98$,

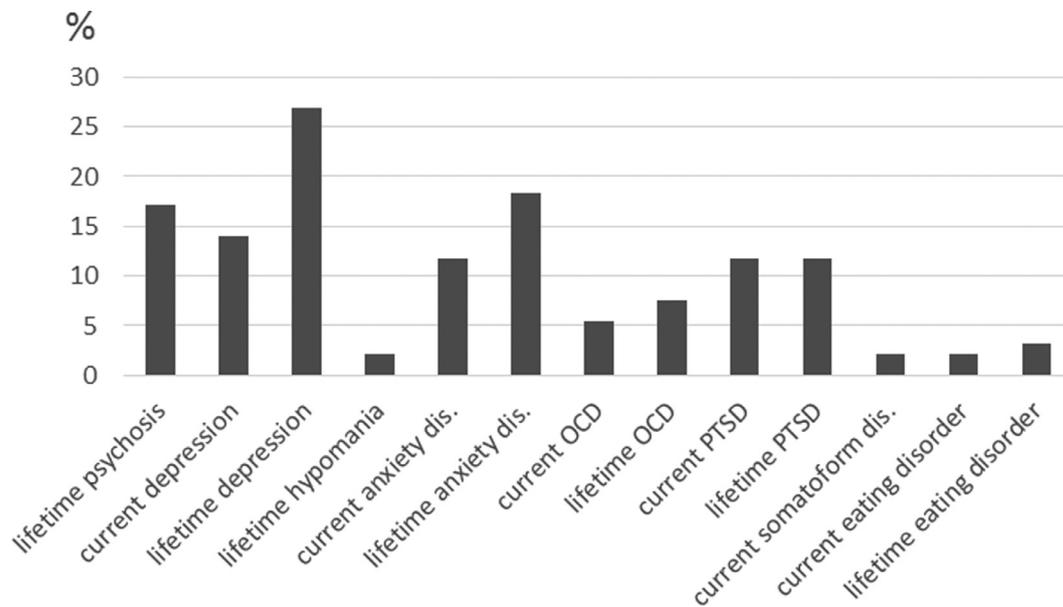


Fig. 1. Overview of all DSM-IV axis I comorbidities (current and lifetime), diagnosed with the semistructured clinical interview.

BF₀₁ = 5.72) nor within those who scored ≥ 30 (p = 0.39).

3.3. Comorbid psychiatric diagnoses at admission

When looking at the admission diagnoses, most of the 108 participants (95%) had another psychiatric ICD diagnosis from chapter V, while only five individuals (4%) had no other psychiatric ICD diagnosis than a diagnosis of F15.2.

Regarding the groups of diagnoses, 92% had at least a second diagnosis from chapter F10–F19, meaning another diagnosis related to substance use or addiction. See Table 1 for a listing of these results. The mean number of additional substance-specific diagnoses was 2.20 (sd = 1.21), with a maximum of 5 additional diagnoses. Within this

Table 1

Frequencies of ICD-10 Chapter F1.X diagnoses from MA users in inpatient treatment programs at the time of admission and discharge.

ICD-10 Diagnosis	Admission n (%)	Discharge n (%)
Substance-specific diagnoses (without MA use or dependence)		
F10.1 alcohol, harmful use	7 (6)	9 (10)
F10.2 alcohol, dependence	23 (21)	24 (22)
F11.1 opioids, harmful use	5 (5)	3 (3)
F11.2 opioids, dependence	10 (9)	10 (9)
F12.1 cannabinoids, harmful use	9 (8)	8 (7)
F12.2 cannabinoids, dependence	67 (62)	63 (58)
F12.3 cannabinoids, mental and behavioral disorder	–	1 (1)
F13.2 sedatives, dependence	4 (4)	1 (1)
F14.1 cocaine, harmful use	2 (2)	–
F14.2 cocaine, dependence	4 (4)	7 (6)
F15.3 psychotic disorder due to stimulant use	–	1 (1)
F15.5 psychotic disorder due to stimulant use	1 (1)	–
F16.1 hallucinogens, harmful use	3 (3)	3 (2.8)
F17.2 tobacco, dependence	65 (60)	66 (61)
F18.2 volatile solvents, dependence	1 (1)	–
F19.1 multiple drug use, harmful use	19 (18)	19 (18)
F19.2 multiple drug use, dependence	9 (8)	3 (3)
F19.5 multiple drug use, psychotic disorder	7 (6)	8 (7)

Note: All admission diagnoses in this table were extracted from pretreatment reports, and all discharge diagnoses were extracted from medical reports of the participating treatment centers after a minimum of 29 weeks of treatment.

comorbidity group, dependency on cannabinoids was the most frequent diagnosis, with 67 participants (62%) having this diagnosis, followed by tobacco dependency (n = 65, 60%) and alcohol dependency (n = 23, 21%).

The mean number of non-substance-specific diagnoses from all participants was 0.55 (sd = 0.77), and 59% did not have any other psychiatric diagnosis, while 30% had one, 8% had two, and 3% had three additional psychiatric diagnoses. Within the group of other psychiatric disorders, 16 participants (15%) were diagnosed with depressive disorder, 13 individuals (12%) had PTSD, 11 subjects (10%) had a hyperkinetic disorder, 7 (6%) had a diagnosis of habit and impulse disorder, 3 (3%) had a diagnosis of paranoid schizophrenia, and 1 (1%) had a specific phobia. Table 2 presents these results in detail.

No impact of age was found on the total number of diagnoses (p = 0.94), addiction diagnoses only (p = 0.59), nor for comorbidities others than addiction (p = 0.94).

3.4. Comorbid psychiatric diagnoses at discharge

In analyzing the diagnoses participants were given at the end of the treatment by the clinicians after several weeks of therapy, all but two patients were either diagnosed again with the addiction of stimulants (F15.2) or the addiction of multiple drug use (F19.2). The other two patients were diagnosed with misuse of stimulants (F15.1). Besides this first addiction diagnosis, 24 participants (22%) got another substance-related diagnosis, 36 subjects (33%) had two other substance-related diagnoses, 31 individuals (29%) had three, 8 participants (7%) had four, and 2 subjects (2%) had five other substance-related diagnoses. This means that only 6% of the sample had just one substance-related diagnosis in total. The mean number of additional substance-specific diagnoses was 2.14 (sd = 1.12), with a maximum of 5 additional diagnoses. See Table 1 for a listing of the results.

When analyzing the non-substance-related comorbidities, most of the 64 participants (59%) were not diagnosed with another psychiatric disorder, while 27 subjects (25%) were diagnosed with one comorbid psychiatric disorder, 10 individuals (9%) with two, 5 participants (5%) with three, and 2 subjects (2%) with four comorbid disorders. The mean number of non-substance-specific diagnoses was 0.65 (sd = 0.96).

No impact of age was found on the total number of diagnoses (p = 0.84), addiction diagnoses only (p = 0.98), or comorbidities other than addiction (p = 0.81).

To complete, paired sample t-tests showed no significant difference

Table 2
Frequencies of ICD-10 Chapter diagnoses, other than F1.X, from MA users in inpatient treatment programs at the time of admission and discharge.

Schizophrenia, schizotypal, and delusional disorders	3(3)	3(3)
F20.0 paranoid schizophrenia	3 (3)	2 (2)
F22.0 delusional disorder	–	1 (1)
Depressive disorders	16(15)	16(15)
F32.0 mild depressive disorder	–	1 (1)
F32.1 moderate depressive episode	8 (7)	6 (6)
F32.2 severe depressive episode without psychotic symptoms	1 (1)	1 (1)
F32.3 severe depressive episode with psychotic symptoms	1 (1)	–
F32.4 major depressive disorder, single episode, in partial remission	–	1 (1)
F32.9 depressive episode, unspecified	1 (1)	–
F33.0 recurrent depressive disorder, current episode mild	2 (1)	2 (1)
F33.1 recurrent depressive disorder, current episode moderate	2 (2)	3 (3)
F33.2 recurrent depressive disorder, current episode severe without psychotic symptoms	1 (1)	1 (1)
F33.4 major depressive disorder, recurrent, in remission	–	1 (1)
Neurotic & stress-related disorders	14(13)	24(23)
F40.0 agoraphobia	–	2 (2)
F40.1 social phobias	–	1 (1)
F40.2 specific (isolated) phobias	1 (1)	–
F41.0 panic disorder	–	3 (3)
F42.1 predominantly compulsive acts (obsessional rituals)	–	1 (1)
F43.1 post-traumatic stress disorder	13 (12)	17 (16)
Behavioral syndromes associated with physiological disturbances and physical factors		3(3)
F55.0 abuse of non-dependence-producing substances	–	2 (2)
F51.5 nightmares	–	1 (1)
Adult personality and behavior disorders	6 (6)	12 (11)
F60.3 emotionally unstable personality disorder	3 (3)	5 (5)
F60.7 dependent personality disorder	–	1 (1)
F61 mixed and other personality disorder	2 (2)	1 (1)
F63 pathological gambling	–	5 (5)
F63.9 habit and impulse disorder, unspecified	1 (1)	–
Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	12 (10)	8 (7)
F90.0 disturbance of activity and attention	9 (8)	7 (6)
F90.1 hyperkinetic conduct disorder	1 (1)	–
F90.9 hyperkinetic disorder, unspecified	1 (1)	1 (1)

Note: All admission diagnoses in this table were extracted from pretreatment reports, and all discharge diagnoses were extracted from medical reports of the participating treatment centers after a minimum of 29 weeks of treatment.

in the number of substance-related ($p = 0.47$) or other psychiatric comorbidities ($p = 0.28$) and the total number of F diagnosis without F15.2 or F19.2 ($p = 0.79$) between admission and dismissal. See a detailed listing of the comorbidities at discharge in [Table 2](#).

3.5. Comorbidities and therapy dropout

Logistic regression showed that the number of substance-specific diagnoses at admission significantly predicted treatment dropout (odds ratio [OR] = 1.5, $p = 0.02$), while the number of substance-specific diagnoses at discharge no longer showed a significant impact on the dropouts ($p = 0.29$). Other psychiatric diagnoses at admission ($p = 0.30$) as well as at discharge ($p = 0.61$) did not predict treatment completion in the regression models.

The total number of diagnoses at admission ($p = 0.06$) and at discharge ($p = 0.21$) can also not be used to predict a dropout. Neither the depression score at admission (BDI-II, $p = 0.56$) nor ADHD score (WURS-k, $p = 0.49$) predicted treatment outcome. Results of logistic regressions are presented in [Table 3](#). Chi² tests did not reveal a significant difference in any of the existing SCID-diagnosed Axis-I comorbidities or treatment completion. See [Table 4](#) for a listing of the results.

Table 3
Univariate logistic regressions between listed comorbid psychiatric disorders at admission/discharge and treatment dropout rate.

	Regression coefficient	Exp(B)	Degrees of freedom	95% confidence interval	p value
Comorbidities at admission					
Substance specific	0.4	1.5	1	1.1; 2.1	.02
Non-substance	–0.3	0.8	1	0.5; 1.3	.30
All comorbidities	0.3	1.4	1	1.0; 1.8	.06
BDI score >0.0	>0.0	1.0	1	0.9; 1.1	.60
WURS-k Score >0.0	>0.0	1.0	1	0.9; 1.0	.05
Comorbidities at discharge					
Substance specific	0.2	1.2	1	0.9; 1.7	.30
Non-substance	0.1	1.1	1	0.7; 1.7	.06
All comorbidities	0.2	1.2	1	0.9; 1.6	.21

Table 4
Chi² tests between SCID I diagnoses and treatment completion show no effects on dropout rates.

Axis-I group	Occurrence	χ ²	df	p-value
Psychosis	lifetime	3.36	1	0.07
	Current	0.75	1	0.78
Depression	Lifetime	0.49	1	0.48
	Current	0.11	1	0.74
Anxiety	Lifetime	0.33	1	0.57
	Current	0.90	1	0.37
OCD	Lifetime	0.83	1	0.36
	Current	0.10	1	0.75
PTSD	Lifetime	0.10	1	0.75
	Current	2.96	1	0.08
Eating disorders	Lifetime	0.07	1	0.79
	Current	2.83	1	0.09
Hypomania	Lifetime	2.83	1	0.09
	Current	2.96	1	0.85

3.6. Gender effects

From the SCID interviews, which were conducted at the time of the admission, six men (7%) had current depression, eight men (9%) had current anxiety disorders, four men (5%) currently suffered from OCD, three men (3%) had a current PTSD, two men (2%) had current eating disorders, and one man (1%) had a current somatoform disorder.

There were also seven women (32%) diagnosed with current depression, three women (14%) with current anxiety disorders, one woman (4%) who currently suffered from OCD, eight women (36%) with a current PTSD, and one woman (4%) with a current somatoform disorder.

Logistic regression models were used to test if the number of substance-specific diagnoses and the number of other psychiatric diagnoses significantly predict the treatment outcome. The number of substance-specific diagnoses in men at admission significantly predicted a treatment dropout (OR = 1.5, $p = 0.02$), while the number of substance-specific diagnoses at discharge in men no longer showed a significant impact on the dropouts ($p = 0.21$). For women, the number of substance-specific diagnoses at admission ($p = 0.97$) or at discharge ($p = 0.52$) did not show a significant impact. In men, other psychiatric diagnoses at admission ($p = 0.25$) as well as at discharge ($p = 0.87$) did not predict treatment outcome in the regression models. Also, in women, there were no significant results regarding the psychiatric diagnoses, other than addiction, at admission ($p = 0.92$) and at discharge ($p = 0.52$).

Comparing the total number of diagnoses at admission ($p = 0.47$) and the admission addiction diagnoses only ($p = 0.38$), there were no significant differences between the gender groups. A significant difference was found in the number of comorbid disorders other than addiction ($t(86) = -3.25$, $p = 0.01$), with women (mean = 0.91, sd = 0.81) having more disorders than men (mean = 0.45, sd = 0.73).

By the time of discharge, there were no longer significant differences between the genders in all diagnoses ($p = 0.68$). However, there were significant differences regarding the comorbidities separately: for addiction-only comorbidities, ($t(86) = 3.60, p < 0.01$), men (mean = 2.31, $sd = 1.06$) had more than women did (mean = 1.45, $sd = 1.06$), and for other comorbidities ($t(16.93) = -2.50, p = 0.02$), men (mean = 0.44, $sd = 0.073$) had fewer than women did (mean = 1.45, $sd = 1.29$). Significantly fewer men currently suffered from major depression ($\chi^2(1) = 12.78, p < 0.01$) and from PTSD ($\chi^2(1) = 24.76, p < 0.01$) than women in the baseline SCID. The average baseline depression scores (BDI-II) between women (mean = 22.21, $sd = 11.44$) and men (mean = 9.55, $sd = 7.61$) also differed significantly ($t(79) = -5.07, p < 0.01$). No differences were seen in anxiety disorders ($p = 0.41$), OCD ($p = 0.91$), somatoform disorders ($p = 0.24$), or eating disorders ($p = 0.49$) for currently existing comorbidities in the SCID interviews and the ADHD score (t -test, WURS-k, $p = 0.23$) between men (mean = 27.27, $sd = 18.78$) and women (mean = 33.63, $sd = 17.61$).

4. Discussion

Decreasing the dropout rate of MA patients to enable better treatment conditions has not been successful so far, because reasons for the high termination rate have not been finally clarified. Because discontinuation of treatment is an ongoing topic, the aim of this study was to provide an overview of the comorbidities in MA abusers and investigate the possible associations with rehabilitation dropout. The study builds on previous research regarding psychiatric comorbidities providing data collected within a German nationwide study in two rehabilitation centers with patients from all over the country. Participants received a diagnosis using well-evaluated instruments, but only the number of substance abuse disorder diagnoses remained a significant predictor of treatment dropout. In general, even if no effects of the number of comorbidities on treatment termination were found, for good clinical practice it remains important to identify psychiatric diagnoses precisely to enable comprehensive treatment and to plan for further treatment after addiction therapy.

In addition, a higher number of additional diagnoses at admission, as noted in participants from HS, did not influence treatment retention since there was no difference within the dropout rates of the centers. Looking at the more sound discharge diagnoses extracted from medical reports of the participating treatment centers after a minimum of 29 weeks of treatment, comorbidity characteristics (i.e., substance related, non-substance related, total number of psychiatric comorbidities) did not show any effect on treatment dropout or completion rate. This is very important for clinical practice, because high dropout rates are often associated with a high comorbidity rate. Thus, it may be that patients presenting a higher number of comorbidities are more often rejected from treatment. But the results do not show evidence of a corresponding influence, which is why the number of comorbidities should not be responsible for an individual prediction of treatment success or dropout. To improve therapeutic success in this field, it is necessary to continue research efforts into the reasons for early discharges. Even if results do not show a respective correlation, it is still important to provide a precise diagnosis and to support patients, not only with further treatments.

Because most MA abusers suffer from psychiatric comorbidities, the results also give an overview about the numbers, composition, and the development of comorbidities over treatment time. First, no significant changes in the comorbidities at admission or discharge were found, meaning a participant will be discharged with approximately the same number of diagnoses with which he was also transferred at admission. Most noticeable changes are multiple-drug use, dependence (F19.2), panic disorder (F41.0), PTSD (F43.1), and pathological gambling (F63). A possible reason for the reduction in F19.2 diagnoses might be the more detailed examination of the "multiple" substances the participants

have been using. An increase in F41.0 as well as F43.1 might be explained by the greater possibility of diagnosis after withdrawal. Regarding panic, Katerndahl and Realini (1999) reported that users of stimulants and multiple drugs are more likely to have panic attacks as well as panic disorders, and the onset of the panic symptoms occurs more often, but not significantly, after the beginning of the drug use. Only 6% of patients reported using the drugs for a self-medication of the panic symptoms. This influence of the substance on the onset of panic symptoms might be one of the main reasons a disorder is not diagnosed while patients are still using drugs as well as the imbalance between admission and discharge, because an ongoing panic disorder diagnosis is possible only within a sufficient time after the withdrawal. Hathaway (2003) additionally reported that 40% of weekly cannabis users start having panic attacks. Looking at the study population, about 60% are diagnosed as cannabis dependent, which further supports the above-mentioned explanation. For PTSD diagnoses, there was an increase between admission and discharge. Teegen and Zumbeck (2000) reported that 42% of substance abusers had at least one trauma experience and 26% suffered from PTSD, which is more than in our sample. This low number could have arisen because MB offers a special trauma treatment program, and no patients from the trauma group, who mainly received trauma treatment, participated in the study.

The participants of this study somehow showed atypical compositions of psychiatric comorbidities (e.g., a very low ADHD rate). In particular, MA, which has a similar neurobiological mode of action (Sandoval et al., 2003) to that of ADHD medication (e.g. methylphenidate), is often used as self-medication (DuPont and Gold, 2007). With stimulants having a high potential for abuse and ADHD patients having a higher rate of a comorbid substance abuse diagnosis than healthy controls (Cortese et al., 2013), a misuse of, for example, MA might more likely lead to dependence in ADHD patients. On the other hand, one main consumption motivation for MA can also be the relatively cheap price, the long half-time period, and its brain reward (DuPont and Gold, 2007), which does not support the self-medication hypothesis. Nevertheless, an ADHD rate of 7% seems very low. Possible reasons for this rate could be that symptoms were raised only at the beginning of treatment with the SCID and the WURS-k. Schmidt and Petermann (2008) mentioned a score of 30 as an indicator for a childhood and ongoing adult ADHD, and the participants of the current study seem to be very close to this threshold, with 47% of the participants scoring 30 or greater. Nevertheless, there was no evidence for a regression between WURS-k and treatment dropout rate. Also, only two participants were diagnosed with a lifetime history of hypomania; we would have expected a higher number based on previous research that showed a correlation of substance use and bipolar disorders (Regier, 1993): 27% of individuals with major depression and 56% with bipolar disorder met criteria for alcohol or drug use. In general, clinicians from the two centers reported that as reference points for their further diagnostic approach, they mostly used the diagnoses of previous treatments or the SCID outcomes, which were assessed only for this study. The WURS-k scores as well as the low number of hypomania cases show the importance of using several diagnostic instruments so as not to overlook a possible diagnosis. Taken together, it remains very difficult to make clear diagnoses at only one time (e.g., the beginning of a treatment), because it is hard to say whether psychiatric symptoms are present only when consuming, during withdrawal, if they are reversible consequences of consumption, or really part of a manifest psychiatric disorder.

Comparing women and men, research finds that men more often use MA than women (Pinotek et al., 2013). The participants of this study were also mostly male, with men having more addiction diagnoses. Women were more likely to have comorbidities (other than substance related) at admission and at discharge. This gender difference might exist because of different consumption motives. Miller et al. (Presser, 2015) found that fitting in ideals of society (children, house, job) is one of the main consumption reasons for women, while men

rather tend to use MA in the sexual environment for enhancement (Thurn et al., 2017) and for changing their mood (Lende et al., 2007).

5. Conclusion

In general, next to substance-related comorbidities, the existence of other comorbid psychiatric disorders can also be very stressful, which is one possible reason for drug consumption. However, according to the results of this study, there is no correlation between an increasing number of comorbidities and higher dropout rate.

The main recommendation is to focus on substance-related comorbidities at admission primarily, as their number can be taken as a predictor of therapy dropout. However, identifying non-substance-related comorbidities is also very important, not just for planning further treatment after discharge. Knowing other comorbidities means providing a more individualized therapy with more specific treatment concepts from which patients seem to benefit. Regarding inpatient treatment, problems related not only to the addiction but also to comorbid disorders can represent a motivation for treatment (Datzer et al., 2002). However, following our results, a high number of comorbid diagnoses should not be decisive for including a patient into rehabilitation or not. According to the results, clinicians should not be afraid of treating patients with psychiatric comorbidities, because no differences in treatment dropout were seen.

6. Limitations and future prospects

This study has some limitations. Testing for consumption motives and personality diagnostics (DSM 5 Axis-II) was not included; therefore, we have to rely on the data given by clinicians and pretreatments. All data were taken from a larger study project that also investigated several other aspects of MA users. Because of requirements for other assessments (for example cognitive tests), this paper mainly focusses on Axis I comorbidities and on individuals currently not suffering from psychosis, because suffering from a current psychosis was an exclusion criteria. Future research is necessary to examine the main influences on treatment dropouts in MA users regarding personality factors and consumption motives.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

Funding sources

LP, FK, LH, MR, SN, and AS are employed and funded by the German Federal Ministry of Health (Project ZMV11-2516DSM216).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.psychres.2019.112505](https://doi.org/10.1016/j.psychres.2019.112505).

References

Bose, J., Hedden, S.L., Lipari, R., Park-Lee, E., 2016. Key substance use and mental health indicators in the United States: rResults from the 2015 national survey on drug use and health. <http://www.samhsa.gov/data/>.

Chen, C.K., Lin, S.K., Sham, P.C., Ball, D., Loh, E.W., Hsiao, C.C., Chiang, Y.L., Ree, S.C., Lee, C.H., Murray, R.M., 2003. Pre-morbid characteristics and co-morbidity of methamphetamine users with and without psychosis. *Psychol. Med.* 33 (8), 1407–1414.

Cortese, S., Holtmann, M., Banaschewski, T., Buitelaar, J., Coghill, D., Danckaerts, M., Dittmann, R.W., Graham, J., Taylor, E., Sergeant, J., 2013. Practitioner review: current best practice in the management of adverse events during treatment with

ADHD medications in children and adolescents. *J. Child Psychol. Psychiatry Allied Discip.* 54 (3), 227–246. <https://doi.org/10.1111/jcpp.12036>.

Darke, S.K., S. McKetin, R., Dufflou, J., 2008. Major physical and psychological harms of methamphetamine use. *Drug Alcohol Rev.* 27 (3), 253–262. <https://doi.org/10.1080/09595230801923702>.

Datzer, S., Härtel-Petri, R., Schiller, M., Wolfersdrof, M., 2002. Rückfallquote methamphetamine abhängiger Patientinnen nach niedrigschwelligem Drogenentzug - Ergebnisse einer mittelfristigen Katamnese. *Suchttherapie* 3, 48–51.

DuPont, R.L., Gold, M.S., 2007. Comorbidity and "self-medication" J. *Addict. Dis.* 26 (Suppl 1), 13–23. https://doi.org/10.1300/J069v26S01_03.

European Monitoring Centre for Drugs and Drug Addiction, 2010. *The State of the Drugs Problem in Europe*. European Union, Luxembourg.

European Monitoring Centre for Drugs and Drug Addiction, 2017. *The State of the Drugs Problem in Europe*. European Union, Luxembourg.

Hathaway, A.D., 2003. Cannabis effects and dependency concerns in long-term frequent users: a missing piece of the public health puzzle. *Addict. Res. Theory* 11 (6), 441–458. <https://doi.org/10.1080/1606635021000041807>.

Hautzinger, M., Kellner, F., Kühner, C., 2009. BDI-II. Beck-Depressions-Inventar. Revision. Pearson, Frankfurt am Main.

Katerndahl, D.A., Realini, J.P., 1999. Relationship between substance abuse and panic attacks. *Addict. Behav.* 24 (5), 731–736. [https://doi.org/10.1016/S0306-4603\(98\)00078-1](https://doi.org/10.1016/S0306-4603(98)00078-1).

Lende, D.H., Leonard, T., Sterk, C.E., Elifson, K., 2007. Functional methamphetamine use: the insider's perspective. *Addict. Res. Theory* 15 (5), 465–477. <https://doi.org/10.1080/16066350701284552>.

Papageorgiou, M., Raza, A., Fraser, S., Nurgali, K., Apostolopoulos, V., 2019. Methamphetamine and its immune-modulating effects. *Maturitas* 121, 13–21. <https://doi.org/10.1016/j.maturitas.2018.12.003>.

Pinotek, D., Kraus, L., Matos, E.G.de, Pabst, A., 2013. Komorbide substanzstörungen in der allgemeinbevölkerung. *SUCHT* 59, 347–354.

Prakash, M.D., Tangalakis, K., Antonipillai, J., Stojanovska, L., Nurgali, K., Apostolopoulos, V., 2017. Methamphetamine: effects on the brain, gut and immune system. *Pharmacol. Res.* 120, 60–67. <https://doi.org/10.1016/j.phrs.2017.03.009>.

Presser L. (Ed.), 2015. Gendered narratives of self, addiction and recovery among women methamphetamine users.

Proebstl, L., Kamp, F., Manz, K., Krause, D., Adorjan, K., Pogarell, O., Koller, G., Soyka, M., Falkai, P., Kambeitz, J., 2019. Effects of stimulant drug use on the dopaminergic system: a systematic review and meta-analysis of in vivo neuroimaging studies. *Eur. Psychiatry* 59, 15–24. <https://doi.org/10.1016/j.eurpsy.2019.03.003>.

Regier, D.A., 1993. The de facto US mental and addictive disorders service system. *Arch. Gen. Psychiatry* 50 (2), 85. <https://doi.org/10.1001/archpsyc.1993.01820140007001>.

Retz-Junginger, P., Retz, W., Blocher, D., Weijers, H.G., Trott, G.E., Wender, P.H., Rössler, M., 2002. Wender utah rating scale (WURS-k) die deutsche kurzform zur retrospektiven erfassung des hyperkinetischen syndroms bei erwachsenen. *Der Nervenarzt* 73 (9), 830–838. <https://doi.org/10.1007/s00115-001-1215-x>.

Salo, R., Flower, K., Kielstein, A., Leamon, M.H., Nordahl, T.E., Galloway, G.P., 2011. Psychiatric comorbidity in methamphetamine dependence. *Psychiatry Res.* 186 (2–3), 356–361. <https://doi.org/10.1016/j.psychres.2010.09.014>.

Sandoval, V., Riddle, E.L., Hanson, G.R., Fleckenstein, A.E., 2003. Methylphenidate alters vesicular monoamine transport and prevents methamphetamine-induced dopaminergic deficits. *J. Pharmacol. Exp. Ther.* 304 (3), 1181–1187. <https://doi.org/10.1124/jpet.102.045005>.

Schmidt, S., Petermann, F., 2008. Testbesprechung. *Zeitschrift für psychiatrie. Psychologie und Psychotherapie* 56 (2), 155–159. <https://doi.org/10.1024/1661-4747.56.2.155>.

Sinha, R., 2001. How does stress increase risk of drug abuse and relapse? *Psychopharmacology* 158 (4), 343–359. <https://doi.org/10.1007/s002130100917>.

Soyka, M., Koller, G., Proebstl, L., Kamp, F., Franke, A., Schmidt, P., Baumgärtner, G., Schacht-Jablonsky, M., Sievert, A., Straif, M., Hamdorf, W., 2017. Prävalenz und therapie bei abhängigkeit von methamphetamine („Crystal“). *Fortschritte der Neurologie-Psychiatrie* 85 (2), 92–99. <https://doi.org/10.1055/s-0042-119862>.

Teegen, F., Zumbek, S., 2000. Prävalenz traumatischer erfahrungen und post-traumatischer belastungsstörung bei substanzabhängigen personen. *Psychotherapeut* 45 (1), 44–49. <https://doi.org/10.1007/s002780050007>.

Thurn, D., Kuntsche, E., Weber, J.A., Wolstein, J., 2017. Development and validation of the amphetamine-type stimulants motive questionnaire in a clinical population. *Front. Psychiatry* 8, 183. <https://doi.org/10.3389/fpsy.2017.00183>.

United Nations Office on Drugs and Crime, 2018. *World Drug report 2018*.

Volkow, N.D., Chang, L., Wang, G.J., Fowler, J.S., Leonido-Yee, M., Franceschi, D., Sedler, M.J., Gatley, S.J., Hitzemann, R., Ding, Y.S., Logan, J., Wong, C., Miller, E.N., 2001. Association of dopamine transporter reduction with psychomotor impairment in methamphetamine abusers. *Am. J. Psychiatry* 158 (3), 377–382. <https://doi.org/10.1176/appi.ajp.158.3.377>.

Wittchen, H.U., Wunderlich, U., Gruschwitz, S., Zaudig, M., 1997. SKID I. Strukturierendes klinisches interview für DSM-IV. Achse I: psychische störungen. Interviewheft Und Beurteilungsheft. Eine deutschsprachige, Erweiterte Bearbeitung Der Amerikanischen Originalversion Des SKID I. Hogrefe, Göttingen.

Zweben, J.E., Cohen, J.B., Christian, D., Galloway, G.P., Salinardi, M., Parent, D., Iguchi, M., 2004. Psychiatric symptoms in methamphetamine users. *Am. J. Addict.* 13 (2), 181–190. <https://doi.org/10.1080/10550490490436055>.