Treatment Outcome, Cognitive Function and Psychopathology in Methamphetamine Users Compared to Other Substance Users

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Abstract

Background: There is an increasing demand of treatment options for methamphetamine users. The present study evaluates differences between methamphetamine users and users of other substances with respect to cognitive function and psychopathology and possible correlates of treatment outcome.

Method: 110 subjects were recruited for an observational longitudinal study from a German inpatient addiction treatment center: 55 patients with methamphetamine dependence and 55 patients with dependence of other substances (OS group). Groups were examined at beginning (baseline) and end of treatment (after six months) with regard to treatment retention, craving, cognitive functioning, psychosocial resources, personality traits, and psychiatric symptoms.

Results: A total drop-out rate of 40% was observed without significant differences. At baseline, Methamphetamine-group subjects had significantly lower intelligence quotient, less years of education, poorer working speed and lower working accuracy and cannabinoid and cocaine use compared to OS-group. Methamphetamine-group subjects showed a significantly lower score of conscientiousness, psychiatric symptoms than subjects from the OS-group. Both groups showed a reduction of craving and depressive symptoms and an improvement of working speed and working accuracy after treatment.

Conclusions: There are differences between methamphetamine users and users of other drugs, but not with regard to the effectiveness of treatment in this inpatient setting.

Introduction

The United Nations estimate that about 27 million people worldwide regularly abuse amphetamine-type stimulants (ATS) [1]. Especially the rising number of people using methamphetamine causes growing concern [2]. Accordingly, figures for methamphetamine users in drug rehabilitation is increasing worldwide and there is a growing need of evidence-based treatment options for methamphetamine users [3]. To date, evidence-based research on the efficacy of treatment programs for methamphetamine users is still limited [4] and the question arises whether established treatment methods for individuals using other substances can be effective for the treatment of methamphetamine dependence as well. This question is important, since -until a few years ago- methamphetamine use played a minor role in German substance treatment services and therefore most methamphetamine users are treated in hospitals or institutions, that still have limited experience with methamphetamine use, but extensive experience with other substance use disorders as for example alcohol, opioids, amphetamine, or cocaine. However, representative studies comparing the characteristics of methamphetamine users to users of other substances are limited. A study based on expert interviews and focus groups to examine the characteristics of methamphetamine consumers showed that they differ from users of other stimulants for example in higher levels of dissocial behavioral (e.g. aggressiveness, impulsiveness, egoism or irritability) as well as a low awareness of their situation, emotional instability, unreliability and many comorbidities [5]. The authors also reported that treatment of methamphetamine users is substantially

affected by their comorbidities and stated, that the provided rehabilitation for methamphetamine users in Germany is inadequate, resulting in a need to adapt the treatment concepts for this group [5]. Another study also showed that methamphetamine use seems to be associated with co-occuring substance use and mental illness [6]. In addition, there are also data indicating that methamphetamine use may lead to neural damage which is commonly associated with persistent cognitive impairment, including deficits in attention, memory and executive function [7]. These results are in line with other studies also demonstrating that methamphetamine users may differ from other substance users with respect to cognitive function [8,9]. This may be of relevance for treatment outcome, since for example Bernhardt et al. noted correlations between outcome in methamphetamine treatment and recovery of cognitive impairment [10].

Another study found an association between a low level of social support and methamphetamine dependence [11]. However, the authors also found an association between moderately (and not distinct) pronounced personality factors (agreeableness, neuroticism, extraversion, conscientiousness and openness) and methamphetamine use [11].

These studies have been mostly of exploratory nature and were investigating exclusively methamphetamine users, but without direct comparison to other drug users. Therefore, the present study aims to examine methamphetamine users' characteristics in comparison with users of other drugs. For this analysis, we focus on factors such as cognition, personality traits, comorbidities, psychiatric symptoms and psychosocial resources and their implication on treatment outcome. Again, there is a lack of studies investigating the treatment outcome of methamphetamine users in existing treatment services, which makes it difficult to deduce specific hypotheses. Based on this limited previous research, one may assume that methamphetamine users have more neuropsychiatric symptoms compared to users of other substances. Specifically, a higher rate of comorbid psychiatric symptoms and disorders, a lower level of cognitive functioning and limited psychosocial resources and finally lower retention rate in treatment in methamphetamine users can be postulated. This exploratory study focuses on these possible differences in primary methamphetamine users compared to users of other substances.

Results

Participants' flow and treatment completion

A total of 110 participants (55 in each group, 89 men and 21 women) with a mean age of 30.95 years (SD= 6.65) were included in the first assessment at T0. There were no statistically significant differences in age (30.0 vs. 32.0 years, p = .12) or gender distribution (76.4% vs. 85.5% males, p= .23) between Methamphetamine- and OS-groups. Out of this original sample, 18 subjects refused to take part in further assessments after T0 and 55 subjects (27 from Methamphetamine-, 28 from OS-group) participated again in the second measurement T1 with a mean age of 30.0 years (SD= 6.43). Again, the majority of T1

subjects was male (45 men, 10 women) and there was no significant difference in gender distribution (p= .50).

From the baseline sample, 66 subjects (60%) completed the treatment while 44 individuals (40%) dropped-out of treatment. Comparison of the Methamphetamine-group and the OS-group revealed no significant difference in drop-out rates (36.4% vs. 43.6%, p= 0.44). There was neither a significant difference in age (p = .19) nor in gender distribution (p= 0.84) between drop-outs and completers.

The reasons for drop-out were as follows: The most common reason for treatment drop-out was at own request (42.2%), followed by violation of institution rules (26.7%), unreported relapse during treatment (24.4%) and transfer to another treatment center (6.7%). There was no significant association in the reasons for drop-out between Methamphetamine and OS-group (p= .21).

Participants remained in treatment for a mean time of 147 days (SD=68). There was a trend towards a longer treatment retention in the Methamphetamine-group compared to OS-group, but this difference failed to reach statistical significance (159 (SD=60) vs. 135 days (SD=73), p = .07). The OS group attended a slightly higher mean number of group sessions (OS: 103 (SD=57); Methamphetamine: 87 (SD= 35), p = .07), while the Methamphetamine-group had a slightly higher mean number of individual therapy sessions (Methamphetamine: 27 (SD= 18); OS 22 (SD=13), p = .08). However, both differences were not statistically significant. A mean treatment duration of 93 days (SD=57) was found among the patients dropping out of treatment.

Baseline comparisons of Methamphetamine and OS-group characteristics

Methamphetamine-group subjects had less years of education than OS-group subjects (p = .048) and showed a significantly lower mean intelligent quotient (Raven`s IQ=93.7) at baseline than the OS-individuals (IQ= 100.1, p = .02, see also Table 3). Methamphetamine-group participants also performed poorer on both measures of the cognitive test battery Cognitrone, resulting in a significantly lower working speed (p = .002) and working accuracy (p = .03) compared to OS-subjects. Methamphetamine- and OS- subjects showed no significant differences with respect to employment (p= .19) or partnership during the last six months prior to admission (p= .46).

Table 1

phases of the therapeutic treatment concept

Therapy phase	Content and therapy frequency	Duration
Admission	Checking the entry requirements, e.g. clean status	Admission day
Entry phase	Diagnostics, self reflection, strengthen and increasing motivation, defining therapy goals, treatment planning	2 weeks
Main phase	Change-, testing and stabilization phase: psychoeducation (2x/week), mindfulness-based relapse prevention (1x/week), trigger analysis (1x/week), individual psychotherapy (50min/week), sports (1x/week), further offers according to the results of diagnostics e.g. nutrition counseling (1x/week), body therapy (1x/week), ergotherapy(1x/week), assertiveness training(1x/week)	22 weeks
Dismissal	Follow-up plan, relapse prevention, arrangement of further contacts with addiction counseling center, doctors and psychotherapists, clarified social situation, e.g. contact to job center and clarified housing situation	2 weeks

Table 2

Study Instruments

Instrument	Description	Assessment
Becks Depression Inventory-II (BDI-II) [22]	21-question multiple-choice self-report inventory measuring the severity of depression. Raw scores were used for analyses.	T0, T1
Cognitrone [23]	Computer administered Test of cognitive working speed and working accuracy (comparisons of geometrical figures). Scores were standardized into T-values according to test norms.	T0, T1
Documentation standards III for the evaluation of the treatment of dependent individuals [24]	Defined items to assess substance use and related factors (e.g. years of substance use, age at use onset, number of withdrawals)	T0
Hamilton Depressive Rating Scale (HAMD) [25]	Clinician-administered depression assessment scale, containing 17 items of symptoms of depression. Time period: past week. Assessed as a semi structured interview. Raw scores were used for analyses.	T0, T1
Inventory of personal psychosocial resources [26]	Self-report questionnaire measuring psychosocial resources in the past and at present based on different scales, e.g. relationship, friends, financial and work situation. A total raw score of all scales measuring the present situation was built and used for analyses.	T0, T1
Mannheimer Craving Scale [27]	Self-report questionnaire with 12 multiple choice items and 4 additional items measuring Craving within the last seven days. Raw scores from the main 12 items were used for analyses.	T0, T1
NEO-Five-Factor-Inventory (NEO-FFI) [28]	Self-report questionnaire with 60 items for the measurement of the so-called “big five” personality traits (neuroticism, extraversion, openness, agreeableness, consciousness). Scores were standardized into T-values according to test norms.	T0
Raven's Standard Progressive Matrices [29]	Nonverbal intelligence test, Computer version. Scores were standardized into IQ values according to test norms	T0
Structured Clinical Interview for DSM-IV Axis I [30]	Diagnostic structured interview to determine the presence of DSM-IV Axis I disorders	T0

Symptom Checklist 90-R (SCL-90R) [31]	Self-report questionnaire assessing symptoms of psychopathology on different scales. For this study two scales were use: intensity of depressive symptoms scale and “Positive Symptom Distress Index” (PSDI), a measure of intensity of present symptoms. Scores of both scales were standardized into T-values according to test norms.	T0, T1
Wender Utah Rating Scale - short Version (Wursk) [32]	Short version (25 items including 4 control items) of a self-report questionnaire assessing retrogradely childhood symptoms of attention deficit hyperactivity disorder. Raw Scores were built from the 21 core items and used for analyses.	T0

Table 3
Comparison between MA- and OS-group at Baseline T0

	MA-group	OS-group	*p*
N	55	55	
Male	42 (76.4%)	47 (85.5%)	p= .23
Age	30.0 (±5.3)	32.0 (±7.7)	p= .12
Number of withdrawals (n=48)	3.0 (±4.1)	3.0 (±4.1)	p= .98
Raven's IQ (MA n=50, OS n=54)	93.7 (±13.5)	100.1 (±13.6)	p= .02
Cognitrone working speed (MA n=53, OS n=54)	49.1 (±8.0)	54.3 (±9.0)	p= .002
Cognitrone accuracy (MA n=53, OS n=54)	43.0 (±8.9)	47.1 (±9.8)	p= .03
Personality factors	n=37	n=42	
Neuroticism	22.8 (±6.7)	25.1 (±9.7)	p= .24
Extraversion	25.0 (±6.0)	25.2 (±7.5)	p= .89
Openness	26.3 (±5.6)	28.6 (±6.7)	p= .11
Agreeableness	26.6 (±4.2)	27.9 (±6.8)	p= .33
Conscientiousness	29.0 (±5.6)	31.9 (±6.6)	p= .04
BDI-II Score (MA n=42, OS n=54)	13.6 (±10.8)	16.8 (±11.3)	p= .17
HAMD Score (MA n=46, OS n=42)	5.3 (±4.8)	8.3 (±7.9)	p= .04
SCL-PSDI Score (MA n=39, OS n=40)	53.5 (±11.1)	59.3 (±10.1)	p= .02

Data displays means and standard deviations (±) or number of participants (education and employment); MA= methamphetamine, OS= other substances; different n result from missing values; BDI-II= Becks Depression Inventory-II; HAMD= Hamilton Depressive Rating Scale; SCL= Symptom Checklist; Wursk= Wender Utah Rating Scale -short Version

	MA-group	OS-group	*p*
Wursk Score	n=36	n=40	p= .56
(MA n=36, OS n=40)	28.6 (±16.7)	30.8 (±15.1)	
Craving	13.9 (±9.5)	14.2 (±8.0)	p= .87
(MA n=39, OS n=40)			
Years of education	*n=52*	*n=50*	p= .048
≤ 9 years	35	24	
≥ 10 years	17	26	
Employment	n= 51	n=48	p= .19
Unemployed	43	33	
Employed	4	7	
Other (e.g. retiree)	4	8	
Ever injected	n=49	n=40	p= .75
	7	4	

Data displays means and standard deviations (±) or number of participants (education and employment); MA= methamphetamine, OS= other substances; different n result from missing values; BDI-II= Becks Depression Inventory-II; HAMD= Hamilton Depressive Rating Scale; SCL= Symptom Checklist; Wursk= Wender Utah Rating Scale -short Version

Participants from the Methamphetamine-group showed a significantly lower score of the personality trait conscientiousness (measured by the NEO-Five-Factor-Inventory) compared with subjects from the OS-group (p = .04). No other personality traits differed significantly between both groups. The OS group showed significantly higher Hamilton Depressive Rating Scale (HAMD) (p= .04) and Symptom Checklist (SCL) depression (p = .03) – but not Beck Depression Inventory-II (BDI- II) (p= .17) – mean scores at treatment begin than the Methamphetamine-group. The OS-group also had a higher mean score of the SCL “Positive Symptom Distress Index” (PSDI), a measure of intensity of present symptoms, compared to the Methamphetamine-group (p = .02). There were no statistically significant differences in Attention Deficit Hyperactivity Disorder (ADHD) scores (p = .56), craving (p= .87) or psychosocial resources (p= .69) at baseline.

As explained, Methamphetamine-group subjects may have had a history of other drug use, but methamphetamine had to be the prior substance. The majority of all subjects also used cannabinoids, but the number of cannabinoid users was significantly higher in the OS-group than in the Methamphetamine-group (p= .04). The OS-group also included a significantly higher number of individuals that used cocaine (p= .001), while there were no differences in the use of other substances.

There was no significant difference between groups concerning the number of previous substance use treatments (p= .98)

Regarding the number of comorbid psychiatric diagnoses (measured by ICD-10), a significantly higher rate in anxiety disorders (p= .03) and somatoform disorders (p< .0001) was found in Methamphetamine-group patients, while there was a higher rate of psychotic disorders in OS- group participants (p= .04, see Table 4).

Table 4
Number of comorbid diagnoses

	MA group n=54	**OS group n=55**	***p***
Depression	11	15	.40
Anxiety disorder	5	0	.03
Eating disorder	0	2	.49
Obsessive-compulsive disorder	0	0	-
Posttraumatic stress disorder	15	12	.47
Personality disorder	11	11	.96
ADHD	6	7	.80
Psychotic disorder	3	10	.042
Somatoform disorder	18	0	<.001

Annotation: Data displays number of participants diagnosed with the respective comorbidity. MA= methamphetamine, OS= other substances, ADHD= Attention deficit and hyperactivity disorder.

Comparisons of groups over time

Mixed ANOVAs were used to compare the cognitive functioning over time and between groups. The working speed significantly improved from T0 to T1 in both groups (p< .001, see also Table 5) and there was a significant group effect for both measurements, showing a better performance in the OS- than in the Methamphetamine group in working speed (p< .001, see figure 2). There was no interaction effect (p= .94). Regarding working accuracy, there also was a significant improvement of performance over time in both groups (p< .001). The OS-group showed a higher working accuracy at both times, but this effect was not statistically significant (p= .43). Again, there was no interaction effect (p= .79, see figure 1). Both

groups showed a significant reduction of the intensity of psychiatric burden, as measured by the SCL-90-R PSDI score, over time ($p < .001$). The OS-group showed a greater decrease than the Methamphetamine-group (see figure 2), but the interaction effect failed statistical significance ($p = .07$). The groups did no longer differ significantly over time ($p = .29$). SCL-90-R depression scores ($p < .001$) and HAMD depression scores ($p = .001$) significantly decreased over time in both groups. However, taking baseline and T1 assessment together, the difference between OS- and Methamphetamine-group was no longer significant (SCL depression score: $p = .09$; HAMD: $p = .09$). Again, no interaction effects were found (SCL depression score: $p = .97$; HAMD: $p = .66$, see figure 3). Analyzing the BDI-II depression scores also revealed a significant effect of time, showing a reduction of depression scores from start to end of treatment ($p < .001$), but without interaction ($p = .81$) or group effect ($p = .56$). Similar results were seen regarding craving scores: we found a significant reduction over time ($p < .001$), without interaction ($p=.94$), and without group effect ($p=.86$). We found a significant increase of psychosocial resources over time ($p = .048$), but again, no significant differences between both groups ($p = .99$) and no interaction effect ($p = .71$)

Table 5
Comparison over time and between groups (ANOVA results)

		MA-group	n	OS-group	n	p
BDI	**T0**	15.31 (±11.55)	26	16.36 (± 12.39)	33	p_{time} ***
	T1	7.27 (± 7.20)		8.97 (± 8.98)		p_{group} n.s. $p_{time}x_{group}$ n.s.
Cognitrone accuracy	**T0**	43.62 (±7.84)	26	44.93 (± 9.85)	28	p_{time} ***
	T1	50.50 (±8.63)		52.54 (± 10.16)		p_{group} n.s. $p_{time}x_{group}$ n.s.
Cognitrone Speed	**T0**	48.81 (±7.68)	26	57.18 (± 9.05)	28	p_{time} ***
	T1	54.08 (±10.04)		62.61 (± 10.88)		p_{group} *** $p_{time}x_{group}$ n.s
HAMD	**T0**	6.52 (±5.36)	25	9.59 (± 9.14)	27	p_{time} ***
	T1	3.60 (±4.77)		5.81 (±5.98)		p_{group} n.s. $p_{time}x_{group}$ n.s.
IPR	**T0**	204.43 (± 36.47)	21	201.78(±33.84)	27	p_{time} *
	T1	215.48 (± 38.71)		217.78 (±54.15)		p_{group} n.s. $p_{time}x_{group}$ n.s.
MaCS	**T0**	14.39 (± 9.81)	23	14.59 (± 6.69)	27	p_{time} ***
	T1	8.57 (± 5.71)		8.96 (± 8.04)		p_{group} n.s. $p_{time}x_{group}$ n.s.
SCL 90R Depression Score	**T0**	58.14 (±9.09)	21	62.70 (± 10.52)	27	p_{time} ***
						p_{group} n.s.

Data displays means and standard deviations; BDI= Becks Depression Inventory-II, MaCs= Mannheimer Craving Scale, IPR= Inventory of personal resources, HAMD= Hamilton Depression Rating Scale, BDI-II= Becks Depression Inventory-II; SCL= Symptom Checklist; $p_{time=}$ effect of time, $p_{group=}$ group effect, $p_{time}{}^{x}{}_{group=}$ interaction effect; **p< 0.05 ***p ≤ 0.001 n.s.= not significant*

		MA-group	n	OS-group	n	p
	T1	50.71 (± 8.19)		55.19 (± 11.55)		$p_{time}x_{group}$ n.s.
SCL 90 R PSDI	**T0**	55.90 (±10.51)	21	61.26 (± 11.40)	27	p_{time} ***
	T1	51.71 (±8.33)		52.61 (± 10.66)		p_{group} n.s. $p_{time}x_{group}$ n.s.

Data displays means and standard deviations; BDI= Becks Depression Inventory-II, MaCs= Mannheimer Craving Scale, IPR= Inventory of personal resources, HAMD= Hamilton Depression Rating Scale, BDI-II= Becks Depression Inventory-II; SCL= Symptom Checklist; $p_{time=}$ effect of time, $p_{group=}$ group effect, $p_{time}{}^{x}{}_{group=}$ interaction effect; **p< 0.05 ***p ≤ 0.001 n.s.= not significant*

Prediction of treatment drop-out

Neuroticism measured at baseline was a significant predictor for treatment drop-out in the whole sample, showing decreasing odds for drop-out with increasing neuroticism scores (OR= .93, 95% CI: [.87, .99], p= .03). No other baseline personality variables predicted treatment drop-out. Higher scores in Cognitrone working accuracy, measured at baseline, also significantly predicted a treatment drop-out (OR= 1.05, 95% CI: [1.0, 1.09], p= .04), while working speed was no significant predictor (p= .20). Raven's IQ (p= .90), Craving at baseline (p= .99), as well as SCL depressive scores (p= .10) were no significant predictors of drop-out.

Discussion

The present study found differences between methamphetamine and other drug users in terms of cognitive function, comorbidities, and personality traits, but no differences regarding treatment outcome and retention. The latter finding suggests that despite the encountered differences between methamphetamine users and other drug users, methamphetamine users do not perform worse than other drug users in currently provided treatments. This result raises the question if there is need for new and specialized treatment options for methamphetamine users. For example, patients may have communicated especially about methamphetamine related situations or consequences when reflecting their use patterns and for example possible relapse situations. In another longitudinal study, we compared the methamphetamine group from this study with another methamphetamine user group, that received a more stimulant specific treatment [12]. We found no difference in treatment retention or long-term relapse rates between both groups, which supports the hypothesis that methamphetamine users do not benefit from a more stimulant specific treatment. We also detected that a high number of methamphetamine users also use other substances. Thus it can be assumed, that existing treatments have a positive effect on the use of these additionally used substances.

Interestingly, the present study revealed a trend (although not statistically significant) towards longer treatment retention of approximately 20 days in the methamphetamine group, which may indicate that methamphetamine users perhaps showed a greater benefit from the investigated treatment in terms of treatment retention or a higher need for treatment. However, with regards to all other treatment outcome measures, we did not find any interaction effects, which suggests that both groups overall benefited from treatment in a similar way. For example, both groups showed a reduction of craving, depression scores and overall psychiatric burden (measured by SCL-90R) and an improvement in working speed and working accuracy as well as an increase of psychosocial resources at the end of the treatment compared to the beginning. Therefore, it can be concluded that a current “treatment as usual” inpatient addiction program is helpful for methamphetamine users *and* users of other substances and that both user groups do not differ from each other in their response to the treatment.

Nevertheless, our study did reveal differences between methamphetamine users and other substance users, for example with respect to cognitive function. As we hypothesized, methamphetamine users had significantly lower baseline intelligence quotient, poorer working speed and lower working accuracy compared to users of other drugs. This finding underlines results from other studies indicating that methamphetamine use can reduce several cognitive functions [8,9]. However, school education was lower in the Methamphetamine-group, raising the question of whether impaired cognitive abilities in the Methamphetamine-group are a reason for or rather a consequence of methamphetamine use. Unfortunately, there are no longitudinal data to further explore this point. Furthermore, the performance of the Methamphetamine user group was still in the average range, when applying the test norms (t-values) and we had no matched control group without drug users to clarify the differences between both groups. Interestingly- and contrary to our assumptions- higher scores in working accuracy at baseline were associated with a higher likelihood for treatment drop-out. Other studies that have examined ADHD patients have found lower accuracy scores as significant predictors of drop out and mild cognitive deficits as a risk factor for treatment discontinuation, which is in contrast to the results of this study [13]. Furthermore, we did not find an effect of working speed and IQ on treatment retention, which makes it difficult to generalize the impact of poorer or better cognitive performance on treatment drop-out.

Again, as assumed, Methamphetamine-patients had a higher rate of comorbid anxiety and somatoform disorders. But contrary to this result, OS- group participants showed a higher rate of psychotic disorders and there were no differences between both groups in terms of other comorbidities. Therefore, different substance use patterns may be associated with different comorbidities, but this does not seem to affect treatment outcome. Future research is needed to clarify, if our results can be observed in other samples as well.

Another unexpected result was the negative association between neuroticism and treatment drop-out. The higher the score for neuroticism, the lower the odds of treatment drop-out. Other studies conclude, contrary to our results, that emotional instability and high neuroticism scores are risk factors for relapse at least in alcohol users [14]. Treatment dropouts in a program for cocaine addiction showed a higher score on histrionic and antisocial scales compared to completers [15]. Since it can be assumed that histrionic as

well as antisocial personality traits tend to be associated with higher neuroticism, this result is also not consistent with our finding. We are not aware of any studies that specifically examined neuroticism as a predictor of addiction treatment dropout.

Our study has several limitations. For example, we did not correct the analyses for multiple testing, as this study was designed to generate hypotheses for future research on possible differences between Methamphetamine- and OS patients.

Furthermore, in the group that used other substances, amphetamine use was not an exclusion criterion. Even though the two substances are very similar, it has been suggested that methamphetamine has a stronger effect on the dopamine transporter mediated cell physiology than maphetamine and therefore leading to a higher addictive potential [16].

Also the illustrated treatment effects are limited to the sample of treatment completers. Regarding the therapeutic effects of the drop-out group, there was no available data for T1, and therefore the treatment effects for the drop-out sample remain unclear. Especially, we did not gain enough information about those patients, who stopped treatment at their own request and therefore dropped out of study. The present study showed that the average time patients spend in treatment before they dropped out is still quite high (around three months). It remains unclear why they did not want to continue the treatment after already investing a lot of time and effort into it. Multiple investigations covering the whole treatment process including the monitoring of treatment alliance can help to gain information on later drop-outs. For example future research may clarify this point by conducting monthly or even weekly surveys on craving, treatment satisfaction and therapeutic relationship, since the latter factors are also known to influence treatment adherence or termination [17–19].

Conclusions

There are differences between methamphetamine users and users of other drugs, but not with regard to the effectiveness of a six-months inpatient addiction treatment. Both groups showed a reduction in psychiatric symptoms over time and improved cognitive function after treatment compared to treatment begin.

Methamphetamine users therefore seem to benefit from existing, stimulant nonspecific treatment options in a similar way than other drug users do.

Methods

Participants and treatment program

All participants were inpatients at a hospital specialized for treatment of substance use disorders (MEDIAN Klinik Mecklenburg) and were recruited by psychologists and physicians during the first two to four weeks after admission. Participation was voluntary and not required for receiving treatment. The

treatment was set up for six months and the interventions were applied as individual and group therapy, while the main focus was on group sessions (five times per week). Table 1 shows details about the treatment concept. Main treatment goals were the analysis of triggers for substance use and the development of new behavioral strategies for coping with craving and other substance related problems. The two-week initial phase aimed at completion of diagnostics, establishment of self-reflection and motivational support and finally defining therapy goals. During the twenty-two-week core treatment phase, interventions as for example psychoeducation, situation and trigger analyses, mindfulness strategies and assertiveness training were applied. The last two weeks focused on relapse prevention and networking for further outpatient treatment. For further details see also Soyka et al. [20].

Inclusion criteria were a history of methamphetamine abuse or addiction (meeting the respective ICD-10 criteria) for the primary methamphetamine user group and a history of abuse or dependence of other substances for the other substances group (OS group). Because polydrug use is very common [21] Methamphetamine-group participants were included when having a history of previous use of other substances, but methamphetamine had to be the primary drug of abuse and the reason for admission to treatment.

Minimum age was 18 years. Exclusion criteria were acute psychotic symptoms, intoxication on test days and insufficient comprehension of study materials or procedure. The study was performed according to the Declaration of Helsinki. Informed written consent was obtained from all participants after a complete and extensive description of the study protocol. The study protocol was approved by the Ethics Committee of the Ludwig-Maximilians-University of Munich, Germany (Project number: 422-16).

All participants were financially reimbursed with 15 Euro after completion of assessments. Routine urine samples and breath alcohol tests were collected to verify use of any substances. These tests were part of the usual hospital practice and were conducted by the clinic staff on a sample basis and in case of suspected substance use.

Study Design

The observational longitudinal study was designed to capture within and between group differences at two time points: “T0” Baseline at the beginning of treatment and “T1” at the end of treatment, after approximately 24 weeks. The T1 assessment took place during the last 3 weeks before discharge and the exact time point varied individually. Both surveys were conducted by trained staff and took place in the MEDIAN clinic Mecklenburg. Data were collected between November 2016 and June 2018 for the Methamphetamine-group and between June 2018 and February 2019 for the OS-group.

Outcome Measures and Instruments

The main outcome of interest was the completion of treatment as scheduled (regular discharge). Individuals stopping treatment prematurely (at own request or as a disciplinary decision) were defined as

dropouts. A positive urine test result was classified as a non-reported relapse, which led to a disciplinary dismissal.

Further outcomes of interest were differences between Methamphetamine- and OS-group and between time points T0 and T1. These differences include craving, cognitive functioning, psychosocial resources, depression and other psychiatric symptoms, as well as personality traits (only measured at baseline). Table 2 displays the used instruments at the respective assessment.

Statistical Analyses

Continuous variables were summarized by their mean (m) and standard deviation (SD), categorical variables by absolute (n) and relative frequencies (%). Group comparisons were performed using chi^2- test (for categorial variables, or in case of small cell numbers, Fisher's exact test) and t-test (continuous variables). Multiple mixed ANOVAs were calculated to compare mean differences between substance groups taking into account both time points (T0 and T1). Since t-tests and ANOVAs are regarded as robust statistical procedures, both methods were also used for variables potentially deviating from the normality assumption. Univariable logistic regression models were applied to investigate the effect of independent factors on treatment drop-out. Odds ratios (OR) are reported together with their 95% confidence intervals (CI). The significance level was set at p= .05 and no p value adjustment for multiple testing was applied in this explorative study. All statistical analyses were conducted in SPSS Version 24.

Declarations

Funding:

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Competing interests:

The authors declare no competing interests.

Data Availability Statement:

Data are available on request.

Ethics declarations:

Ethics approval was made by the ethic committee of LMU Munich (Project number: 422-16)

Author contributions:

G.F., G.K. and M.S. designed the study. N.B., L.P. L.H., M.R., M.S-J., and W.H. performed study experiments. A.K.M. did the statistical analyses. F.K. wrote the manuscript. D.K. and S.N. contributed to writing and critical revisions. All authors read and approved the final manuscript.

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Figures

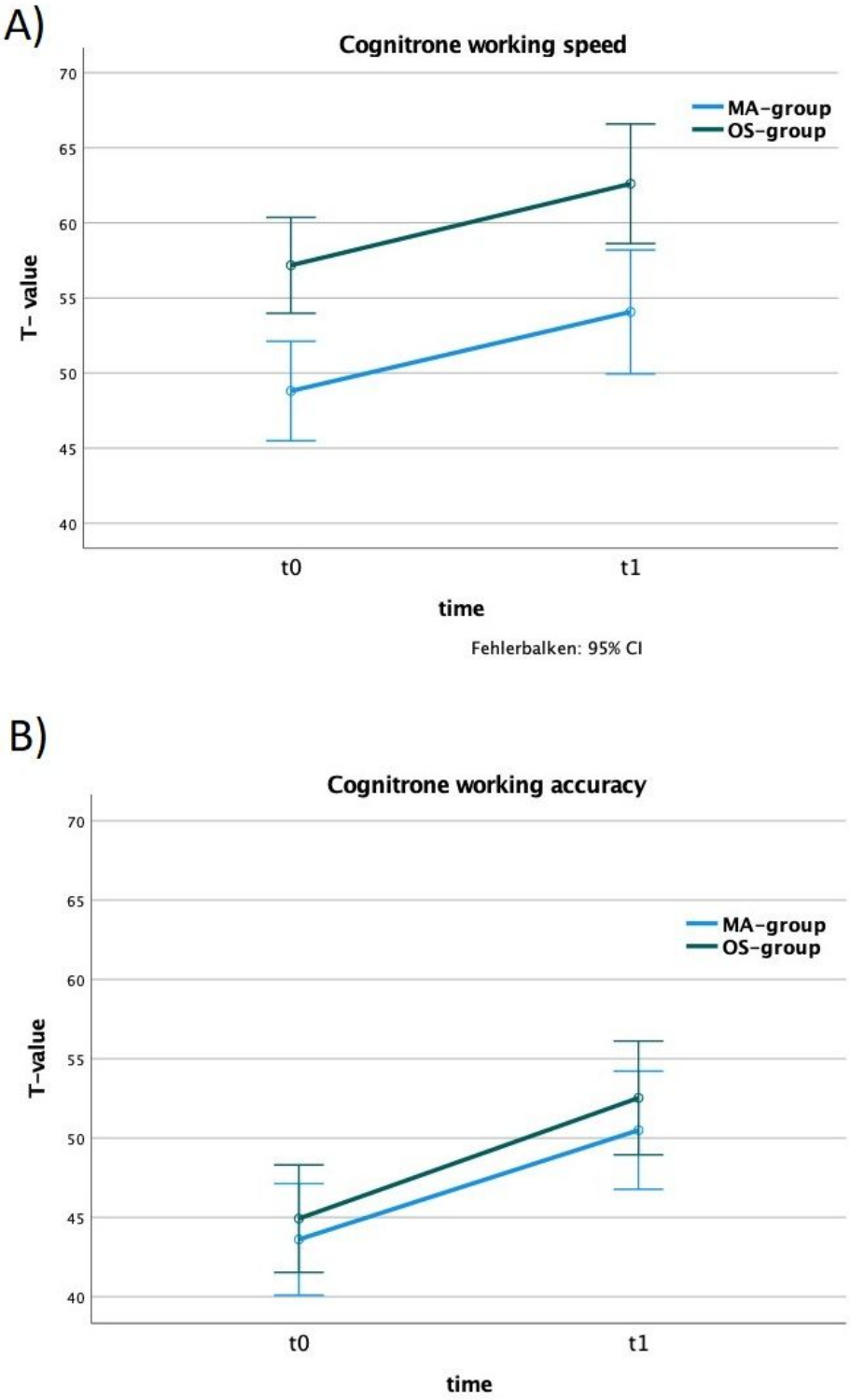

Figure 1

A) Working speed over time and between groups (error bars represent 95% CI) B) Working accuracy over time and between groups (error bars represent 95% CI) legend: MA= methamphetamine, OS= other substances

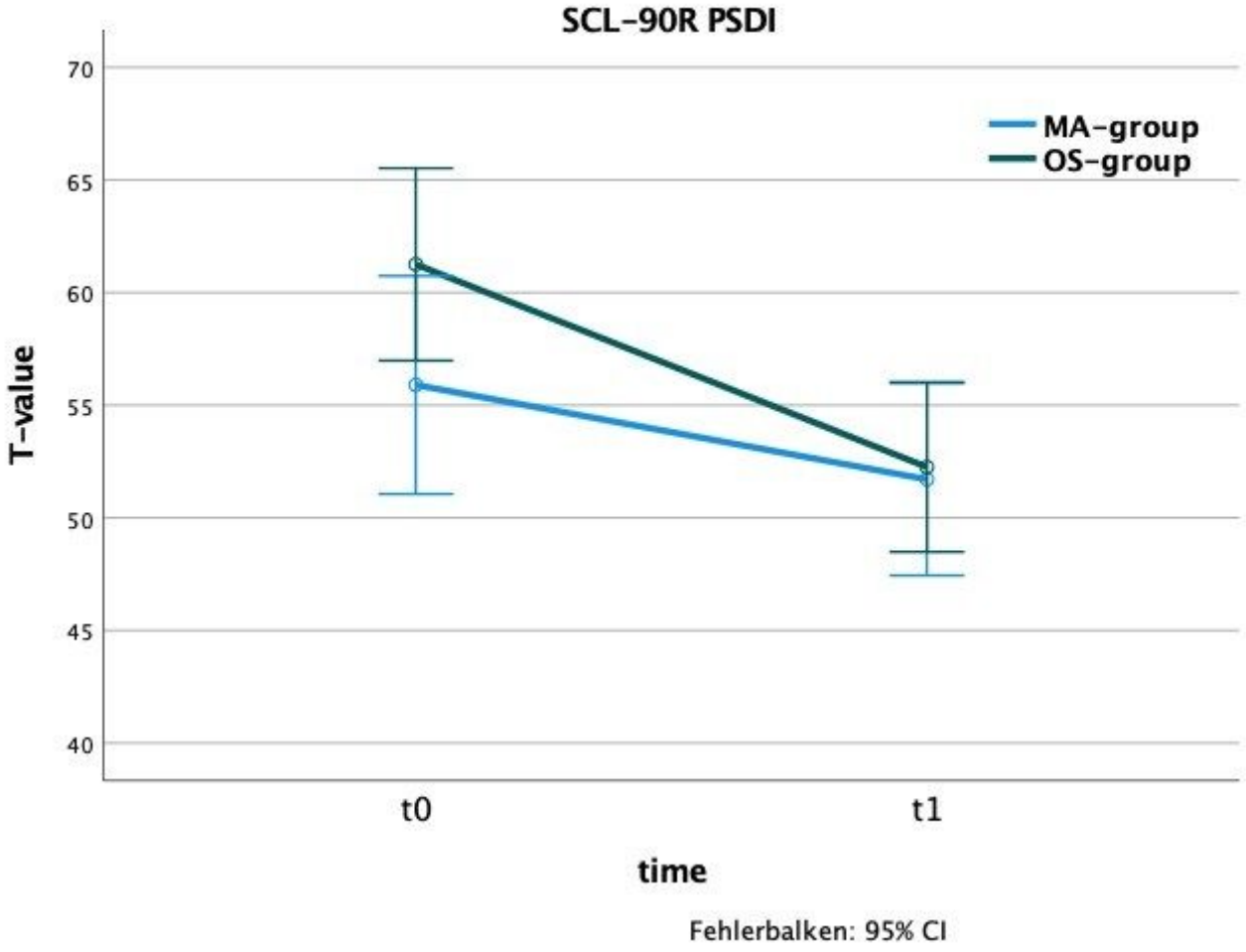

Figure 2

Positive Symptom Distress Index (SCL-90-R) over time and between groups (error bars represent 95% CI)
legend: MA= methamphetamine, OS= other substances

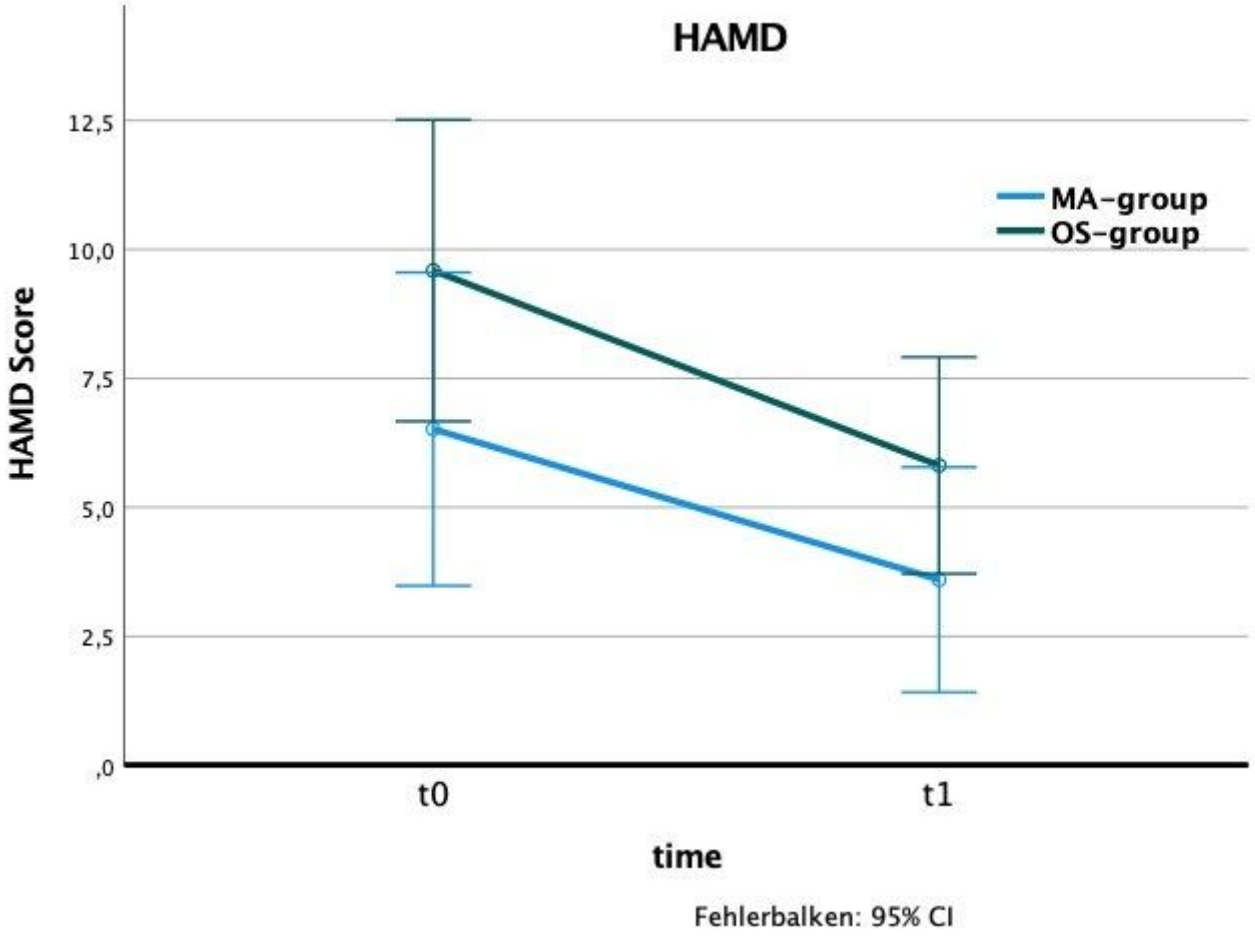

Figure 3

HAMD scores over time and between groups (error bars represent 95% CI) legend: MA= methamphetamine, OS= other substances, HAMD= Hamilton Depression Rating Scale