



Methamphetamine withdrawal and the restoration of cognitive functions – a study over a course of 6 months abstinence

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ABSTRACT

A continuously rising consumption of methamphetamine (MA) has been suggested to be associated with increasing cognitive dysfunction. The objective of this study was to investigate associations between cognitive functions and gender, drug using patterns and treatment-attending profiles of recently abstinent MA users over the course of six months abstinence. Data were collected from 108 participants in two inpatient rehabilitation centers. The mean duration of MA use was 11.5 years. Interviews and cognitive tests (cognitron, Stroop, TMT, nback) were performed right after the withdrawal and again after approx. six months of abstinence. Comparisons and explorative analyses between the groups (gender, primary MA/ multidrug users, early dropouts/ completers) regarding cognitive variables were performed. At baseline a significant decline in general neuropsychological functioning and attention/concentration after ongoing years of consumption were found. After a period of six months abstinence, cognitive performances remained stable or improved significantly for cognitron percentile and cognitive flexibility. Normal cognitive functions were measured in former MA users after acute withdrawal which remained stable and partly improved in those patients who refrained from substance abuse over six months. Continued long-term MA intake was the only identified indicator of poorer cognitive performance. These results point towards a regain of cognitive performance in patients abstinent from MA.

1. Introduction

The consumption of the amphetamine type stimulant methamphetamine (MA) has risen rapidly in the past few years with an estimated annual prevalence of 0.7% worldwide (United Nations Office on Drugs and Crime, 2017). In the European Union, the lifetime use is 1.0% (European Monitoring Centre for Drugs and Drug Addiction, 2017). The stimulating effects of MA are dose dependent, including e.g. hypervigilance, tachycardia, reduced hunger and psychological and psychiatric effects (Hart et al., 2001; Cruickshank and Dyer, 2009). MA consumption causes a downregulation of dopamine receptors and transporters in

the brain (Ashok et al., 2017; Proebstl et al., 2019). This acute effect can lead to a general downregulation of receptors to compensate the higher dopamine release under drug effects (Volkow et al., 2001). The human brain does adapt to such changes (Björklund and Dunnett, 2007), which might be one reason for the development of cognitive impairments since a remodelling of brain circuits can cause an impairment of cognitive functions (Mizoguchi and Yamada, 2019). Current research still discusses if cognitive deficits, especially executive functions, are affected by the neurobiological effects of MA consumption (Dean et al., 2013). It has been demonstrated that MA dependent individuals showed a reduced capacity in complex decision making

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tasks, working memory and cognitive flexibility compared to healthy controls (van der Plas et al., 2009). Current MA users show poorer performances than previous MA users (Sabrini et al., 2019) but it remains unclear for how long these impairments remain or even whether they completely recover (Stock et al., 2019). Suffering from impaired cognitive functions can contribute to a variety of difficulties in everyday functioning (Morgan et al., 2014). It remains unclear whether the risk of cognitive impairment increases with long-term ongoing use of MA and especially whether cognitive performances recover at all within abstinence (Proebstl et al., 2018). During the very early period of MA abstinence, research has shown that after 4–9 days MA dependent individuals had significantly decreased cognitive performances, especially with regard to processing speed. Impairments persisted even after one month of abstinence (Simon et al., 2010).

By contrast, for long-term sobriety a regain of normal cognitive functions has been found in a sample of MA users who remained abstinent for one year. At baseline, both current and former MA users displayed cognitive deficits, measured as reduced processing speed (Iudicello et al., 2010). Cognitive problems in early or later phases of abstinence can lead to an increased probability of a relapse of substance abuse. Neuroimaging studies have demonstrated structural brain changes (corticostriatal dysfunction, altered brain connectivity) in MA dependent patients while performing cognitive tasks. These abnormalities are associated with addiction-related phenotypes (e.g. poor inhibitory control, maladaptive decision making, impulsivity, cognitive inflexibility), which can develop from transmitter deficiencies and could impact therapy responses (London et al., 2015).

So far, factors influencing cognition remain unclear in MA patients. This study explores typical characteristics of cognitive impairments in a MA using cohort in order to investigate potential differences between women and men as well as patients from different consumer groups (mainly MA users versus multidrug users including MA); in addition, individuals using MA and cannabis versus individuals using MA as a main substance within their multidrug use, and finally differences between subjects who completed their rehabilitation treatment and those who dropped out early.

Altogether, the aim of this study is to shed some light on the association between cognitive performance, drug-using patterns and treatment attending profiles of former MA dependent patients after acute withdrawal, and its changes over the course of six months abstinence.

2. Material and methods

2.1. Participants

All participants were recruited as formerly MA consuming inpatients from two different rehabilitation centers in Germany: MEDIAN Clinic Mecklenburg and the District Hospital Hochstadt. The socio-demographic characteristics of the participants did not differ across the centers, except for age. Hochstadt offers more therapy places financed by the pension insurance, which may explain the higher age of the participants treated there (Kamp et al., 2019).

Inclusion criteria were previous MA consumption, a negative drug urine screen on the test day(s) and a minimum age of 18 years. Subjects with known psychotic disorders and those unable to read or understand the tests properly were excluded. All participants received € 50 as compensation. The ethics commission of the LMU Munich approved the study protocol and all participants signed an informed consent.

The German Federal Ministry of Health provided funding for the study. Detailed information about the treatment can be found in Soyka et al. (Soyka et al., 2017). Briefly, after acute withdrawal, all study subjects were undergoing a continuous inpatient treatment in closed MA groups, meaning every included participant had a history of MA use as a main substance. In order to get precise information about the sample's structure, the participants were grouped for analyses based on gender, consumption habits and treatment completion. Regarding the

consumption habits, participants were divided into two groups. One group was called “primary methamphetamine consumers” (MC) and were only diagnosed with ICD-10 (American Medical Association, 2016) F15 (stimulants) diagnoses. Cannabis (ICD-10 F12) was an allowed substance in the MC group too, since the majority of MA consumers are using it (inpatient: 70%), probably because of its sedative effects (Soyka et al., 2017). The other group was called “poly-substance abusers” (POLY) which included participants with additional addiction diagnoses other than F15 and F12 only. Thus, all participants of the POLY group had been using MA as well.

2.2. Design

The neurocognitive assessment was performed twice. Baseline measurements (T0) took place after participants had finished their acute withdrawal phase and started their inpatient treatment in a specialised rehabilitation center. The follow-up evaluation (T1) took place six months after treatment completion. The following survey instruments were used: The Documentation Standards for Addiction is a freely accessible German evaluation questionnaire about socio-demographic and addiction related variables (Deutsche Gesellschaft für Suchtforschung, 2001), which was conducted by trained study personnel. All subsequent tests were processed on a computer (Schuhfried, 1992) with an average duration of ten minutes per test. Ravens Standard Progressive Matrices (Raven, 2000) was used to derive an intelligence quotient (IQ). Cognitronne (Schuhfried, 2007) was used to test attention and concentration skills influencing all kind of performances (Wagner and Karner, 2003). Here, the total score of all reactions made during the seven minutes of processing time as well as the percentiles were used to allow a comparison with the standard sample of the tests. Both variables provide information about the cognitive processing speed corresponding to the quantity in the tested person's performance. Within the n-back verbal test (Schelling and Schuri, 2016) working memory and capacity were assessed by showing various stimuli which the subjects must recall. For calculations standard T-values of the number of correct responses within 7 min were used. The Stroop test (Schuhfried, 1999) reflects the capacity to maintain a course of action in the face of intrusion by other stimuli. For calculations standard T-values representing the naming and reading interference were used. While the first test counts the time until items are properly named, the second test stands for the time to read common words printed in different colours (Scarpina and Tagini, 2017). The Trail Making Test (TMT) (Rodewald et al., 2017) assesses general neuropsychological functioning, cognitive processing speed and eye-hand coordination with cognitive flexibility (Tischler and Petermann, 2010). Here the times and T-values for tasks A and B and the percentiles representing the cognitive flexibility of the participants were used. Before all testings and during the rehabilitation, urine screenings were performed at irregular intervals to check the participants' abstinence status. In addition, the subjects were asked about their abstinence status at regular intervals.

2.3. Statistical analysis

Participants were attributed to different groups according to their gender, consumption habits (MC or POLY) and the treatment completion status (unsuccessful dropouts or completers). Not all participants completed all of the tests, some discontinued during the measurement or did not want to give information on some variable, which is why the sample size can vary between the different analyses. All complete screenings were included for the calculations. Participants were only excluded if data were not complete. Sociodemographic characteristics of the participants are provided separately for the entire cohort and for the different groups. Normality assumption was roughly checked by plotting histogrammes while all variables were deemed to be normally distributed. T-tests were used to compare means of continuous normally

distributed variables such as age, baseline IQ score and duration of consumption. Categorical variables such as gender, marital status, children, living situation in the last six months, education, employment and retention rates of the treatment were compared using chi-squared tests. Correlation was assessed by means of Pearson's correlation coefficient. Univariable linear regression was used to identify possible associations between the duration of MA use and performances in cognitive tests. All analyses were conducted with SPSS 25 while a significance level of $p = 0.05$ was used. Due to the explorative character of this study, no p value adjustment for multiple testing was considered.

3. Results

3.1. Sociodemographic results and social factors

A total of 108 participants was included in the analysis, of which 79.6% were male ($n = 86$). The MC group ($n = 44$) consisted of 51 men (79.7%) and the POLY group ($n = 62$) of 35 men (79.5%). A total of 44 participants dropped out, 23 of them in the MC (35.9%) and 21 (47.7%) in the POLY group, respectively. In the completer group ($n = 64$) there were 51 men (79.7%) and in the dropout group ($n = 44$) 35 men (79.5%). There was no significant difference in the gender distribution between MC group and POLY group ($p = 0.98$) or completers and dropouts ($p = 0.99$). The mean age in the entire cohort was 31.67 years ($sd = 7.7$, range: 18–56). Women's mean age was 32.1 years ($sd = 6.3$) and men's 31.6 years ($sd = 8.0$). The mean age in the MC group was 30.33 ($sd = 6.4$) and in the POLY group 33.4 ($sd = 8.9$). The mean age in the group of treatment completers was 31.8 ($sd = 7.8$) and in the group of dropouts 31.4 ($sd = 7.7$). There were no significant differences in the mean age between both genders ($p = 0.75$), the MC and POLY group ($p = 0.57$), or the termination ($p = 0.77$) groups.

The level of education revealed that 73 subjects (67.6%) reported to have left German secondary school after six years or less, 28 participants (25.9%) stated to have stayed at school at least for 10 years leaving German secondary school with a certificate; 3 subjects (2.8%) reported to have a German high-school diploma. There was no significant association between education level and duration of MA consumption ($p = 0.53$). In addition, no significantly different education levels were found in the gender ($p = 0.33$), the consumer ($p = 0.41$) and the termination groups ($p = 0.74$).

3.2. Duration of methamphetamine consumption

The overall duration of MA consumption reached a mean of 11.5 years. There were no significant differences in the consumption duration in the gender ($mean_{women} = 12.5$, $mean_{men} = 11.3$, $p = 0.44$), consumer ($mean_{MC} = 11.5$, $mean_{POLY} = 11.6$, $p = 0.91$) and termination groups ($mean_{compl} = 11.3$, $mean_{dropout} = 11.9$, $p = 0.56$).

3.3. Neurocognitive analysis at baseline

IQ testing revealed a $mean_{IQ}$ of 92 points in all study participants. No significant correlation was found for duration of consumption and IQ ($p = 0.85$). Also, there were no significant IQ differences regarding the gender groups ($mean_{women} = 90.3$, $mean_{men} = 93.5$, $p = 0.35$), the consumer ($mean_{MC} = 93.0$, $mean_{POLY} = 94.0$, $p = 0.47$) or the completer ($mean_{compl} = 92.4$, $mean_{dropout} = 93.6$, $p = 0.67$) groups.

With respect to cognitive testing, the result of the cognitronne showed a $mean_{total\ reactions}$ of 410.1 and a $mean_{percentile}$ of 51.1. The nback verbal revealed $mean_{T\ value} = 54.5$ for correct variables and the Stroop was completed with $mean_{T\ value} = 46.6$ in reading interference and $mean_{T\ value} = 50.8$ in naming interference. In the TMT, subjects showed a result of $mean_{time} = 19.5$ s in task A and 31.1 s in task B. The cognitive flexibility was $mean_{percentile} = 48.7$. See Table 1 for a detailed listing of the results.

Significant weak to moderate correlations were found between the duration of consumption and TMTA-time ($r = 0.45$, $p < 0.01$, $R^2 = 0.2$) and the cognitronne percentile ($r = -0.21$, $p = 0.03$, $R^2 = 0.05$), see Fig. 1 for scatterplots. No significant correlations were found for duration of consumption and $cognitronne_{total-reactions}$ ($p = 0.07$), nback ($p = 0.58$), reading interference ($p = 0.62$), naming interference ($p = 0.09$), TMTB ($p = 0.36$) or cognitive flexibility ($p = 0.39$). See Table 2 for a detailed listing of the results.

Significant differences were found for women scoring higher in reading interference than men ($t(35) = -2.02$, $p = 0.05$) while the MC group performed better in TMTA than the POLY group ($t(38) = -2.60$, $p = 0.01$). See Table 3 for baseline group scorings.

3.4. Neurocognitive analysis at follow-up

The cognitive test results after 6 months of abstinence regarding the cognitronne showed a $mean_{total\ reactions}$ of 457.7 and $mean_{percentile}$ of 64.1. The n back verbal revealed a $mean_{T-value} = 55.4$ for correct variables and the Stroop was completed with $mean_{T-value} = 45.8$ in reading interference and $mean_{T-value} = 47.9$ in naming interference. In the TMT the subjects showed a result of $mean_{time} = 19.6$ s in A and 30.0 s in B. The cognitive flexibility was $mean_{percentile} = 50.6$. See Table 1 for a detailed listing of the results. A significant moderate negative correlation was found between the duration of consumption and the cognitronne percentile ($r = -0.44$, $p = 0.01$, $R^2 = 0.2$) see Fig. 2 for the scatterplot. No significant correlations were found for the duration of consumption and $cognitronne_{total-reactions}$ ($p = 0.06$), nback ($p = 0.73$), reading interference ($p = 0.83$), naming interference ($p = 0.73$), TMTB ($p = 0.44$) or cognitive flexibility ($p = 0.98$). See Table 2 for a detailed listing of the results. A significant difference for comparing dropouts and completers regarding the $cognitronne_{total-reactions}$ ($p < 0.01$) was found with the completers showing more reactions. No other significant differences between women and men or the MC and POLY groups were found. See Table 4 for follow-up group scorings.

In order to assess longitudinal effects, baseline values were compared with the follow-up measurements. Significant improvements were found for $cognitronne_{total\ reactions}$ ($p < 0.00$), the $cognitronne_{percentile}$ ($p < .01$) and the TMTB, which also represents the cognitive flexibility ($p < 0.01$). No significant differences were found for the n back task ($p = 0.81$), reading interference ($p = 0.40$), naming interference ($p = 0.13$), TMT A ($p = 0.87$) and B ($p = 0.72$) times.

4. Discussion

The present study measured neurocognitive performances in former MA dependent patients after acute withdrawal and after six months of abstinence. At the baseline measurements, all participants showed average cognitive scores and the scores partly improved over the time of abstinence. The sociodemographic characteristics of the study cohort are similar to the study by Milin et al. (Milin et al., 2014) so that we consider the individuals participating in this study as a typical sample of MA users. The typical MA consumer in our study was 32 years old, male, single or unmarried, living alone and having a lower type of education without employment. This is why we believe the results of this study can be transferred to other MA using populations.

Over the course of six months abstinence, the cognitive performance remained stable and partly improved regarding the scorings. All total and subgroup results were on average levels (compared to standard samples), showing that discontinuation of MA leads to cognitive abilities improving over time. In addition, we showed with a significant positive correlation that the longer patients had consumed MA, the worse they performed on cognitive tests (general neurophysiological functioning and cognitive processing speed ($TMTA_{time}$), together with a significant negative correlation that attention and concentration worsen with longer MA consume ($cognitronne_{percentile}$). The average duration of MA consumption in the cohort was almost 12 years, which

Table 1
Listing of cognitive scorings and comparisons of baseline and follow-up measurements.

		n	Baseline ^a		Follow-Up ^b		p value ^c	
			Mean	Min/max (sd)	n	Mean		Min/max (sd)
Cognitron	reactions	106	410.1	176.0/725.0 (99.3)	33	457.7	284.0/674.0 (105.2)	<0.001***
	percentile		51.1	1.0/100.0 (27.1)		64.1	11.0/100.0 (28.8)	0.001**
N back	T value	41	54.5	20.0/80.0 (9.5)	25	55.4	36.0/80.0 (17.9)	0.81
Stroop	reading interference	37	46.6	27.0/64.0 (9.5)	25	45.8	27.0/73.0 (11.2)	0.40
	naming interference		50.8	34.0/66.0 (8.8)		49.3	29.0/60.0 (12.6)	0.13
TMT	A ^c	39	47.3	35.0/55.0 (4.8)	25	47.3	35.0/55.0 (5.8)	0.18
	B ^c		47.8	32.0/59.0 (7.2)		51.9	39.0/68.0(7.2)	0.001**
	cognitive flexibility ^d		48.7	3.0/98.0 (29.2)		50.6	23.0/91.0 (24.9)	0.51

^a after withdrawal.
^b after about 6 months of abstinence.
^c T values.
^d mean percentile representing the cognitive flexibility.
^e *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

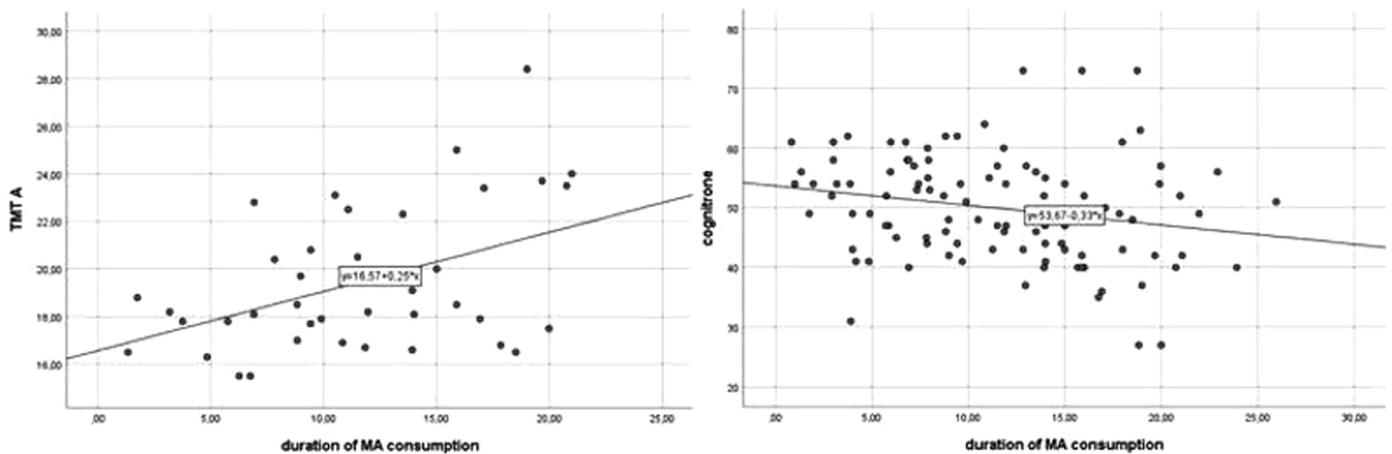


Fig. 1. Scatterplots for correlations between baseline TMT A time in seconds ($n = 39, r = 0.45, p < 0.01$)/cognitron percentile ($n = 106, r = -0.21, p = 0.03$) and the duration of methamphetamine consumption in years.

Table 2
Univariable linear regressions regarding the duration of methamphetamine consumption and results of cognitive tests for baseline and follow up measurements.

Baseline		Regression coefficient	Standard error	T value	p-value ^c	CI (95%)	R ²
TMT	A – time ^a	0.81	0.27	3.06	<0.01**	0.3, 1.4	0.20
	B – time ^b	0.09	0.10	0.92	0.36	-0.11, 0.30	0.02
	cognitive flexibility	-0.03	0.03	-0.87	0.39	-0.09, 0.04	0.02
Cognitron	percentile	-0.05	0.02	-2.18	0.03*	-0.09, -0.01	0.05
	reactions	-0.01	0.01	-1.80	0.07	-0.02, 0.00	0.03
N back verbal	T value	-0.03	0.04	-0.57	0.58	-0.11, 0.06	0.01
Stroop	reading interference	0.05	0.09	0.49	0.62	-0.15, 0.24	0.01
	naming interference	-0.17	0.09	-1.72	0.90	-0.37, 0.03	0.10
Follow up		Regression coefficient	Standard error	T value	p-value ^c	CI (95%)	R ²
TMT	A - time	-0.01	0.02	-0.37	0.72	-0.05, 0.03	0.00
	B - time	-0.01	0.02	-0.35	0.72	-0.05, 0.03	0.00
	cognitive flexibility	-0.01	0.02	-0.39	0.71	-0.04, 0.03	0.00
Cognitron	percentile	-0.01	0.01	-1.67	0.09	-0.03, 0.00	0.03
	reactions	-0.01	0.01	-1.57	0.12	-0.01, 0.00	0.03
N back verbal	T value	-0.02	0.06	-0.34	0.73	-0.16, 0.11	0.01
Stroop	reading interference	0.03	0.13	0.22	0.83	-0.23, 0.30	0.00
	naming interference	-0.04	0.11	-0.35	0.73	-0.25, 0.18	0.00

^a time in seconds.
^b mean percentile representing the cognitive flexibility.
^c *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

Table 3
Baseline: group-wise listing of cognitive scorings and comparisons of specific methamphetamine user groups.

		Men			Women			p value ^c
		n	Mean	Min/max (sd)	n	Mean	Min/max (sd)	
Cognitrone	reactions	84	410.3	176.0/725.0 (101.6)	22	409.2	299.0/627.0 (92.4)	0.96
	percentile		51.4	1.0/100.0 (26.9)		50.1	16.0/99.0 (28.1)	0.85
N back verbal	T value	32	56.4	34.0/80.0 (19.3)	10	48.6	20.0/80 (22.5)	0.29
Stroop	reading interference	28	44.9	27.0/64.0 (9.4)	9	51.9	36.0/62.0 (7.8)	0.05
	naming interference		50.5	35.0/66.0 (8.4)		51.8	34.0/66.0 (10.2)	0.71
TMT	A – time ^a	31	19.1	15.5/28.0 (2.9)	9	20.9	17.8/25.0 (8.5)	0.11
	B – time ^a		30.9	52.6/201.0 (8.5)		31.8	21.5/50.6 (9.7)	0.78
	cognitive flexibility ^b		47.8	3.0/95.0 (28.7)		51.1	7.0/98.0 (32.6)	0.78

		POLY group			MC group			p value ^c
		n	Mean	Min/max (sd)	n	Mean	Min/max (sd)	
Cognitrone	reactions	62	405.4	176.0/716.0 (103.1)	44	416.7	190.0/725.9 (94.6)	0.57
	percentile		49.1	1.0/100.0 (27.9)		53.9	1.0/100.0 (25.86)	0.38
N back verbal	T value	25	55.6	20.0/80.0 (20.9)	17	52.9	190.0/725.0 (94.2)	0.66
Stroop	reading interference	23	45.4	34.0/56.0 (7.9)	14	48.6	27.0/64.0 (11.6)	0.32
	naming interference		48.7	34.0/66.0 (8.2)		54.2	35.0/66.0 (8.95)	0.07
TMT	A – time ^a	23	18.5	15.5/25 (2.6)	17	20.8	16.5/28.4 (3.1)	0.01*
	B – time ^a		31.4	21.5/51.2 (9.1)		30.7	20.1/52.6 (30.7)	0.80
	cognitive flexibility ^b		46.5	3.0/98.0 (30.1)		51.7	3.0/ 95.0 (28.6)	0.59

		Dropout group			Completer group			p value ^c
		n	Mean	Min/max (sd)	n	Mean	Min/max (sd)	
Cognitrone	reactions	44	410.7	176.0/716.0 (104.8)	62	409.7	190.0/725.0 (96.2)	0.96
	percentile		51.5	1.0/100.0 (27.2)		50.5	1.0/ 100.0 (26.4)	0.85
N back verbal	T value	12	44.6	20.0/80.0 (18.8)	30	58.1	34.0/80.0 (19.7)	0.06
Stroop	reading interference	10	46.9	34.0/59.0 (8.1)	27	46.4	27.0/64.0 (10.1)	0.89
	naming interference		53.4	43.0/66.0 (8.6)		49.9	34.0/66.0 (8.9)	0.28
TMT	A – time ^a	11	20.1	16.7/23.7 (2.5)	11	19.3	15.5/28.4 (3.2)	0.44
	B – time ^a		29.3	20.1/46.5 (8.9)		31.7	22.0/52.6 (8.6)	0.44
	cognitive flexibility ^b		59.6	3.9/95.0 (31.9)		44.6	3.0/98.0 (27.9)	0.15

^a time in seconds.
^b mean percentile representing the cognitive flexibility.
^c *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

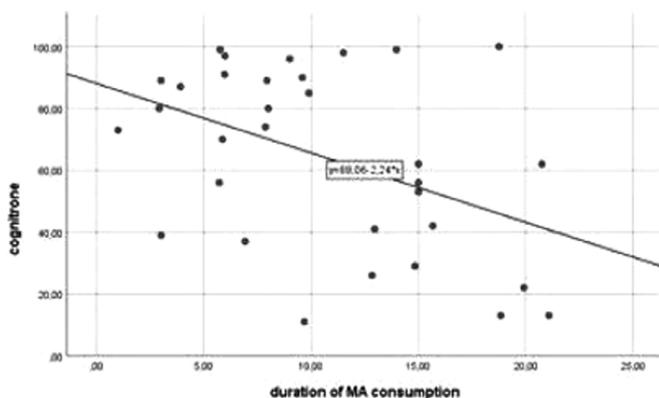


Fig. 2. Scatterplots for correlations between follow-up cognitrone percentile and duration of methamphetamine consumption in years ($n = 32, r = -0.44, p = 0.01$).

is rather long and therefore it is remarkable to find normal cognitive tests in this long-term MA using cohort during a period of abstinence. The association between years of MA consumption and decreasing cognitive performance is in line with previous results (van der Plas et al., 2009). In addition, in our study it could be shown that over a six months period of abstinence cognitive improvement is possible in the areas of attention and concentration skills as well as in cognitive flexibility. Previous literature on cognitive performance in former MA addicts remains inconclusive. Especially during the early course of abstinence, cognitive functions were demonstrated to be reduced in patients who were abstinent from MA for one month (Simon et al., 2010). Zhong et al. (Zhong et al., 2016) also measured cognitive

performance in abstinent MA patients over a course of six months. At the first assessment they found that individuals with MA dependency had lower results in cognitive tests and verbal memory, working memory and problem solving compared to healthy controls. However, similar to our study, six months later they discovered an improvement in some areas like executive function and verbal memory (Zhong et al., 2016). Furthermore, a recovery of cognitive functions was shown in a cohort of abstinent MA dependent individuals followed up for a year. In a global neuropsychological assessment at baseline, MA addicted individuals performed worse than healthy controls. One year later, those subjects still abstinent from MA had similar test results to controls. Therefore, these results point towards a possible restoration of cognitive functions during a period of abstinence (Iudicello et al., 2010).

In most aspects such as age, marital status, educations levels, current employment situation, duration of MA consumption and termination rates there were no differences between MA dependent men and women. This leads to the supposition that MA consumers of both genders can be treated equally regarding those variables. At baseline, a significant difference was found for reading interference with women showing better skills in maintaining a course of action than men. However, at six months of abstinence, this difference vanished (Stroop test). This result is not consistent with prior research (Golden, 1974; Houx et al., 1993) but points towards higher task-focus abilities in women of our cohort. Contrasting findings have been described also for a MA dependent cohort: Van der Plas previously measured impairments in decision making, which were more prevalent in female than in male MA users (van der Plas et al., 2009).

There were also no differences regarding the duration of consumption, which could have been an indicator for more damage in the brain, but this does not support women scoring better in the Stroop

Table 4
Follow-up: group-wise listing of cognitive scorings and comparisons of specific methamphetamine user groups.

		Men			Women			p value ^c
		n	Mean	Min/max (sd)	n	Mean	Min/max (sd)	
Cognitrone	reactions	26	462.2	284.0/619.0 (95.5)	7	440.9	293.0/674.0 (143.4)	0.64
	percentile		66.9	11.0/99.0 (27.3)		53.7	13.0/100.0 (33.9)	0.29
N back verbal	T value	18	55.3	38.0/80.0 (16.3)	7	55.6	36.0/80 (22.9)	0.98
Stroop	reading interference	18	44.9	27.0/62.0 (9.9)	7	48.1	40.0/62.0 (7.5)	0.45
	naming interference		47.4	29.0/73.0 (10.9)		49.3	29.0/60.0 (12.6)	0.71
TMT	A – time ^a	4	19.3	16.6/21.9 (2.4)	2	20.2	16.0/24.5 (6.0)	0.87
	B – time ^a		29.0	201.0/52.6 (8.5)		32.1	29.2/34.9 (4.0)	0.55
	cognitive flexibility ^b		47.8	3.0/95.0 (28.7)		38.0	28.0/48.0 (14.1)	0.44

		POLY group			MC group			p value ^c
		n	Mean	Min/max (sd)	n	Mean	Min/max (sd)	
Cognitrone	reactions	15	476.3	292.0/619.0 (110.6)	18	442.2	284.0/674.0 (101.0)	0.36
	percentile		68.5	13.0/99.0 (29.9)		60.4	11.0/100.0 (28.1)	0.43
N back verbal	T value	11	60.1	36.0/80.0 (19.7)	14	51.6	36.0/80 (16.1)	0.25
Stroop	reading interference	11	44.7	27.0/62.0 (12.2)	14	46.6	39.0/62.0 (6.6)	0.65
	naming interference		49.1	29.0/73.0 (13.4)		47.0	29.0/60.0 (9.5)	0.65
TMT	A – time ^a	5	19.9	16.0/24.5 (3.6)	1	18.1	18.1/18.1 (0)	–
	B – time ^a		31.0	25.8/37.6 (5.1)		25.2	25.2/25.2 (0)	–
	cognitive flexibility ^b		48.0	23.0/91.0 (26.8)		64.0	64.0/64.0 (0)	–

		Drop-out group			Completer group			p value ^c
		n	Mean	Min/max (sd)	n	Mean	Min/max (sd)	
Cognitrone	reactions	3	386.3	369.0/409.0 (20.5)	30	464.8	284.0/674.0 (107.7)	<0.001**
	percentile		44.7	37.0/56.0 (10.0)		66.0	11.0/100.0 (29.3)	0.23
N back verbal	T value	1	36.0	36.0/36.0 (0)	24	56.2	36.0/80.0 (17.8)	–
Stroop	reading interference	1	42.0	42.0/42.0 (0)	24	46.0	27.0/62.0 (9.5)	–
	naming interference		60.0	60.0/60.0 (0)		47.4	29.0/73.0 (11.2)	–
TMT	A – time ^a	1	24.5	24.5/24.5 (0)	5	18.6	16.0/21.9 (2.6)	–
	B – time ^a		34.9	34.9/34.9 (0)		29.0	25.2/37.6 (5.0)	–
	cognitive flexibility ^b		48.0	48.0/48.0 (0)		51.2	23.0/91.0 (27.8)	–

^a time in seconds.

^b mean percentile representing cognitive flexibility.

^c *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

distinction.

Furthermore, there are almost no differences between multiple drug users or primary MA users. One difference was found for the cognitive processing speed (TMTA) at baseline. The MC group performed better than the POLY group, which may be due to the lower number of consumed substances, but the follow up results do not show this difference anymore. This leads to the conclusion that the different consumer groups adjust during the six months of abstinence. This result shows that a polytox drug use is not affecting a consumer's cognition in a more harmful way than primary MA consumption, unless the cognitive processing speed happens to be lower at the time after acute withdrawal.

Overall, no significant differences were found regarding the treatment completers and the early dropouts. Participants who dropped out early stated to have consumed one year longer than participants who completed the therapy. Further research is necessary to identify predictors for early therapy termination and relapses, which are one of the main reasons for the high dropout rate in addiction treatment.

5. Limitations

The present study has several limitations. Firstly, the study population consisted only of MA dependent patients and no healthy controls were included. Therefore, the test results could only be compared to norm values of the tests. However, the norm values are representative of the general population and thus comparable to healthy controls included in other studies. Secondly, the separation of the two groups into primary MA consumers and multiple substance users did not evaluate the intake of multiple substances in the primary MA group taken longer than one year ago. This could have made the two groups more similar to each other and thus prevented us from finding significant differences

between the groups. Thirdly, the influence of other mental comorbidities on overall cognitive performances was not included. To crosscheck the abstinence status, regular urine tests and interviews took place. Nevertheless, there is no guarantee that all participants were really abstinent during the entire time of the treatment.

6. Conclusion

This study shows that in recently abstinent MA subjects cognitive performance reached normal levels and that this performance remained stable and even partly improved in those patients who refrained from substance abuse over six months. Long-term consumption of MA seems to be an indicator for worse cognitive performance. Finally, these results point towards recoverable cognitive abilities in patients abstinent from MA.

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Declaration of Competing Interest

None.

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Supplementary materials

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