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Decision making of individuals with heroin addiction receiving opioid maintenance treatment compared to early abstinent users



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ABSTRACT

Background and aims: Individuals with heroin addiction are prone to dysfunctional decision-making. They frequently choose the short-term rewarding option of drug intake despite experiencing long-term negative consequences. Opioid maintenance treatment (OMT) is the most common treatment of heroin addiction.

Methods: In this study, 38 individuals in an early stage of abstinence from heroin addiction (ESA-HA individuals) at the end of inpatient detoxification treatment and 41 individuals in long-term OMT were examined. Decision-making was assessed by (I) a modified version of the Iowa Gambling Task (IGT) with drug-related stimuli focusing on decision-making under ambiguity and (II) the Game of Dice Task (GDT) assessing decision-making under objective risk.

Results: OMT-individuals showed significantly better performance in the IGT than the ESA-HA-individuals. They also showed significantly less craving under exposure of drug-related pictures. In the GDT, OMT-individuals showed significantly less risky decision-making than ESA-HA-individuals.

Conclusion: The results suggest that patients receiving OMT show better functional decision-making and lower craving reactions. It could be assumed that the effectiveness of OMT in preventing relapse is linked to better decision-making and lower craving among these patients.

1. Introduction

Heroin addiction is one form of opioid dependence or opioid use disorder (OUD) and is a severe mental disorder with a chronic course. It is associated with an increased mortality, comorbid somatic disorders, e.g., hepatitis C, and social problems, such as criminal activity and unemployment (Hser et al., 2001). Research has already illustrated that individuals with opioid abuse, such as heroin and opiate consumption, are prone to behave riskier in everyday life. Individuals frequently showed criminal behavior and poor physical and mental health, even if they experience long-term negative consequences such as impaired social functioning or stigmatization (Biernacki et al., 2016; Brand et al., 2008; De Maeyer et al., 2010, 2011). Individuals with OUD seem to prefer immediate rewards instead of delayed rewards even if it results

in negative consequences in the long-term (Franken and Muris, 2005; Lemenager et al., 2011; Rivalan et al., 2009). Furthermore, on a neuropsychological level, deficits in executive functions and cognitive impulsivity seem to be main attributes of OUD (e.g., Verdejo-García et al., 2007; Verdejo-García and Pérez-García, 2007). In the systematic review by Moningka et al. (2019), neuroimaging studies show functional and structural impairments associated with cognitive components (e.g., prefrontal cortex) as well as deficits in reward processing and emotion/stress regulation in individuals suffering from OUD (Verdejo-García et al., 2007; Verdejo-García and Pérez-García, 2007). Yang et al. (2015) investigated response inhibition in individuals with OUD, healthy controls, and individuals receiving methadone maintenance treatment. The results showed impairments in evaluating and inhibiting inappropriate behavior in both patient groups compared to

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healthy controls. The authors additionally concluded that methadone maintenance treatment may improve response inhibition and further cognitive functions (Yang et al., 2015), which is line with Soyka et al. (2008).

Impairments in decision-making abilities are considered further key mechanisms in the development and maintenance of substance-use disorders (Bechara, 2005). The meta-analysis by Biernacki et al. (2016) as well as further empirical studies by Dom et al. (2005) and Lemenager et al. (2011) outline that OUD is related to decision-making deficits. Research defines different decision-making situations based on the knowledge about probabilities and consequences in each situation, named decision-making under objective risk and decision-making under ambiguity (Brand et al., 2006; Schiebener and Brand, 2015). Decision-making situations under objective risk provide information about probabilities, outcomes, and potential wins and losses. Based on dual-process theories, theoretical models (Brand et al., 2006; Evans, 2003; Kahneman, 2003), and empirical findings in healthy individuals and several groups of individuals with neurological diseases and psychological disorders (including substance-use disorders and behavioral addictions), decision-making under objective risk is associated with executive functions, working memory, and feedback processing (comprehensive review in Schiebener and Brand, 2015). In contrast, decision-making under ambiguity is associated more intensively with feedback processing, feelings and hunches as well as implicit learning processes (Brand et al., 2006; Damasio, 1994, 2004). Decision-making impairments have been reported in individuals with OUD for both decision-making under objective risk (e.g., Brand et al., 2008) and decision-making under ambiguity (e.g., Biernacki et al., 2016). The results outline that current opioid users show impairments in decision-making under ambiguity compared to healthy controls. These impairments were not related to the length of abstinence, since there were also no differences between current users and abstinent users with OUD (Biernacki et al., 2016).

Further central components, which are associated with the repeated consumption of illegal drugs and other substances, are cue reactivity and craving. Cue reactivity is defined as the increased vulnerability of individuals regarding drug-related cues (Carter and Tiffany, 1999; Kiefer et al., 2013). Furthermore, cue reactivity is an important motivational-emotional and physiological basis to experience craving (Everitt and Robbins, 2005). The experience of craving describes the subjective desire or urge towards a substance and is an important diagnostic criterion of substance-use disorders (Drummond, 2001; Kavanagh and Connor, 2013; Tiffany and Wray, 2012). Several studies have already provided evidence for the central role of cue reactivity and craving in OUD (e.g., Fatseas et al., 2011; Moningka et al., 2019), which was still relevant for individuals receiving methadone maintenance treatment (Yen et al., 2016). Neuroimaging studies outline greater activation in the prefrontal cortex when performing inhibitory control tasks, which seem to be related to impaired control over craving reactions (Fu et al., 2008; Schmidt et al., 2013; Yucel et al., 2007).

There are also studies showing that decision-making, cue reactivity and craving interact in concert in explaining the course of substance-use disorders (Goldstein and Volkow, 2011). For studying the potential impact of cue reactivity and other affective processes on decision-making under ambiguity, a modified version of the Iowa Gambling Task (Bechara et al., 1994) has been introduced by Pittig et al. (2014). They investigated participants with spider phobia and demonstrated that these individuals tend to avoid card decks that are linked to (task-irrelevant) spider pictures even if avoiding these card decks results in negative consequences in long-term. This finding is consistent with the assumption that reactivity on phobia-related stimuli interferes with advantageous decision-making. Laier et al. (2014) have illustrated the relevance of specific pornographic cues in making decisions under ambiguity. The authors showed that particularly those men with high sexual excitability continue choosing card decks with (task-irrelevant) pornographic pictures although these decisions are linked to high

monetary losses. Addiction research assumes that enhanced sensitivity towards drug-related cues increases the likelihood of craving and relapse (Koob and Volkow, 2010). Additionally, empirical as well as theoretical considerations suppose an interaction of cognitive as well as affective responses such as decision-making and craving reactions in substance use disorder such as OUD (Bechara, 2005; Moningka et al., 2019).

The most common treatment of heroin addiction is opioid maintenance treatment (OMT) including methadone or buprenorphine. According to its basic principle, it is assumed that the medical administration of an opioid with a long elimination half-life once daily in OMT suppresses heroin withdrawal symptoms and heroin craving (De Vos et al., 1999; Fareed et al., 2011). Bart (2012) showed that methadone and buprenorphine maintenance treatment seem to be the best forms of OUD treatment and are associated with retention in treatment programs, reductions of drug abuse, improved social functioning, and decreased craving. Individuals who are suffering from negative consequences due to their heroin addiction can reduce heroin use by pharmaceutically induced reductions of craving. The reduction of heroin use is associated with a reduction of risky drug administration, criminal activities as well as social problems (Newman and Whitehill, 1979). However, Li et al. (2015) showed that individuals receiving OMT heightened neural responses when being confronted with drug-related cues compared to neutral cues and compared to healthy controls. It could be assumed that this may normalize after sustained abstinence or pharmacotherapy. Soyka et al. (2008) also conclude that substitution therapy could be a possibility to improve cognitive functions. However, up to now there is an ongoing debate whether OMT is just a controlled addiction with reduction of heroin use and its negative sequelae by administration of a medical opioid instead of heroin. Considering ethical standards, it is difficult to investigate the effects of long-term OMT on changes of mental dispositions of individuals with OUD in a controlled setting. Nevertheless, former research more often focused on the comparison between current heroin users and healthy controls or individuals receiving OMT and healthy controls, respectively (e.g., Biernacki et al., 2016; Li et al., 2015; Mintzer and Stitzer, 2002; Soyka et al., 2008). The comparison of long-term OMT with those abstinent individuals without OMT would allow outlining differences regarding cognitive components such as impulsivity, attentional bias to drug-related stimuli, and decision-making. In this study, we investigate decision-making in individuals with heroin addiction at an early stage of abstinence (ESA-HA) compared to individuals with former heroin addiction who receive OMT. Furthermore, the interplay of decision-making capabilities and the additional effect when being confronted with drug-related cues will be addressed. Investigating the effect of OMT results in a better understanding of underlying treatment mechanisms, which could have positive implications for further research and treatment programs. In the first hypothesis, we assume that OMT-individuals experience less craving compared to ESA-HA-individuals. Investigating decision-making behavior, we secondly hypothesize that OMT-individuals show a) a better decision-making performance under ambiguity in a modified Iowa Gambling Task confronted with drug-related stimuli and b) a less risky decision-making under objective risk conditions compared to ESA-HA-individuals.

2. Methods

2.1. Participants

The sample of the current study consisted of 79 individuals with heroin addiction according to DSM-IV at point of data collection (American Psychiatric Association, 1994). These criteria are still valid with regard to the DSM-5 (American Psychiatric Association, 2013). Overall, the sample consists of two groups (see Table 1). The first group includes 38 individuals of a detoxification ward for drug addicts of a psychiatric university hospital, who, up to admission, used heroin

Table 1
Demographic variables and information of the sample.

| | | Overall sample (N = 79) | OMT-individuals (n = 41) | ESA-HA-individuals (n = 38) | Group comparisons |
|---|---------------|-------------------------|--------------------------|-----------------------------|---------------------------|
| Gender | male / female | 65 / 14 | 31 / 10 | 34 / 4 | $\chi^2 = 2.60, p = .107$ |
| Age | <i>M (SD)</i> | 40.47 (8.94) | 42.80 (8.31) | 37.95 (9.00) | $t(77) = 2.49, p = .015$ |
| Time of substitution (in years) | <i>M (SD)</i> | | 7.87 (5.42) | | |
| Injection phobia | Frequency | 5 (6.33%) | 0 | 5 (13.16%) | $\chi^2 = 5.76, p = .016$ |
| Intravenous drug abuse^a | Frequency | 58 (73.42%) | 35 (85.37%) | 23 (60.53%) | $\chi^2 = 6.24, p = .013$ |

^a The variable illustrates the proportion of participants as well as the percentage distribution of those participants who demonstrated an intravenous form of drug consumption compared to the inhaled form of consumption. The form of drug consumption refers to the time before withdrawal syndrome treatment or substitution treatment. The OMT-individuals were free of charge for at least 30 days at the time of investigation.

regularly (group of heroin-addicted individuals at an early stage of complete opioid abstinence, ESA-HA individuals). These individuals already completed an inpatient or partly inpatient withdrawal treatment during the study. They did not receive any withdrawal-relieving medication at the time of investigation. Even if the participants consumed additional substances previously, heroin was the main substance. At the time of investigation, the detoxification was completed, defined as a negative drug screening (except THC), no more administration of opioids to reduce withdrawal symptoms and no even minor withdrawal symptoms upon clinical examination for at least three days. The second group includes 41 individuals in OMT using racemic methadone, levomethadone, or Suboxone® (combination of buprenorphine and naloxone), mentioned as OMT-individuals.

The following exclusion criteria were defined for both groups: history or current manifestation of neurological and psychiatric diseases including all neurodegenerative diseases and all neurological conditions that could potentially affect brain functioning, e.g., a positive HIV status, a history or current presence of schizophrenia, and the current medication of another co-morbid axis I psychiatric disorder excluding supportive night medication like mirtazapine. In the OMT-group, a comorbid alcohol dependence, the current abuse of other drugs (apart from cannabis) or abuse of medication during the last 30 days before examination (checked by regular urine drug tests) were additional exclusion criteria.

All participants signed informed consent in accordance with the declaration of Helsinki prior to the investigation and did not receive financial compensation for their participation in the study. The local ethics committee has approved the study.

2.2. Instruments

2.2.1. Craving assessment

To assess craving, ten drug-related pictures were presented. The pictures showed drug-related stimuli such as the substance itself, the preparation of heroin intake, and the moment of injecting heroin intravenously. The pictures were presented on a computer screen. For each picture the participant rated subjective craving on a scale ranging from 1 (= no craving) to 10 (= maximum craving).

2.2.2. Decision-making under ambiguity

The Iowa Gambling Task (IGT) is a task to measure decision-making under ambiguity (Bechara et al., 1994, 2000). For the current study, a new modified version of the computerized IGT was used (IGTmod). The IGT contains four decks of cards (A, B, C, D) with 40 cards per deck. The participants are not informed about the duration of the game/number of trials and the rules for gains and losses. They get instruction to maximize the starting capital of €2000 and that some decks are more advantageous than other decks. During the task, the participants have to learn by feedback processing, which decks are advantageous or disadvantageous. In each of 100 trials, the participants are supposed to choose one card of any deck. Following each choice, participants win a specific amount of fictitious money but occasionally also lose a specific amount. Decks A and B are considered disadvantageous, because they

lead to high immediate gains but to even higher occasional losses resulting in a negative long-term outcome. In contrast, decks C and D are considered advantageous because they yield low immediate gains but also low occasional losses resulting in a positive long-term balance. During the entire task, the actual capital is shown numerically and displayed by two colored bars. A green bar indicates a positive balance and a red bar a negative balance.

In the IGTmod, drug-related pictures and neutral pictures are presented on the backsides of the cards. Drug-related pictures were the same as used for the craving measure described in section 2.2.1, and neutral pictures were taken from the International Affect Pictures System (IAPS; Lang et al., 2008). In version 1, drug-related pictures are on the backsides of the advantageous decks (drug-picture-CD group), and neutral pictures are placed on the disadvantageous decks (A and B). In version 2, the presentation of drug-related and neutral pictures is inverted (drug-picture-AB group) (see Fig. 1). For analyzing IGTmod performance, a net score is calculated by subtracting the number of disadvantageous selections from the number of advantageous selections (net score = (C + D) - (A + B)). Accordingly, a positive net score indicates advantageous decision-making. Besides the overall score, the performance in the IGT could be also analyzed by calculating the net score of the first twenty trials (net score of the first block) and of the last twenty trials (net score of the fifth block) (see also Fig. 2).

2.2.3. Decision-making under risk

In order to measure decision-making under risk, the Game of Dice Task (GDT; Brand et al., 2005) was used. This computerized task explicitly expresses to the participants the rules for (fictitious) monetary gains and losses and fixed winning probabilities in a decision-making situation. The goal of this task is to maximize the fictitious starting capital of €1000 within the 18 trials in which one virtual die is thrown. In each trial, the participants bet on one single number or on combinations of two, three, or four numbers. Each option is associated with explicit and stable gains and losses constantly presented on the screen. The participants get the information that the game finishes after 18 trials and that they can continue playing even if they have a negative balance. The choice of a single number (e.g., “3”) provides a gain or loss of €1000 (winning probability = 16.67%). If the chosen number (e.g., “3”) is thrown, the fictitious gain is €1000. If one of the five other numbers not chosen is thrown (e.g., “1”, “2”, “4”, “5” or “6”), the fictitious loss is €1000. A further alternative is to choose a combination of two numbers (winning probability = 33.33%) associated with a possible gain of €500 but also with a loss of €500 in case one of the numbers not chosen is thrown. Participants also have the choice of selecting a combination of three numbers (winning probability = 50%) linked to a gain or loss of €200 and a combination of four numbers (winning probability = 66.67%), which will lead to a gain or loss of €100. After each decision, a visual and acoustic feedback about the amount of gain (colored green) or loss (colored red) is presented. The remaining trials and the current capital are permanently shown on the screen. The two categories (one single number and the combination of two numbers) are defined as “high risk”, since the winning probability is less than 34%. The other two categories (combination of three and

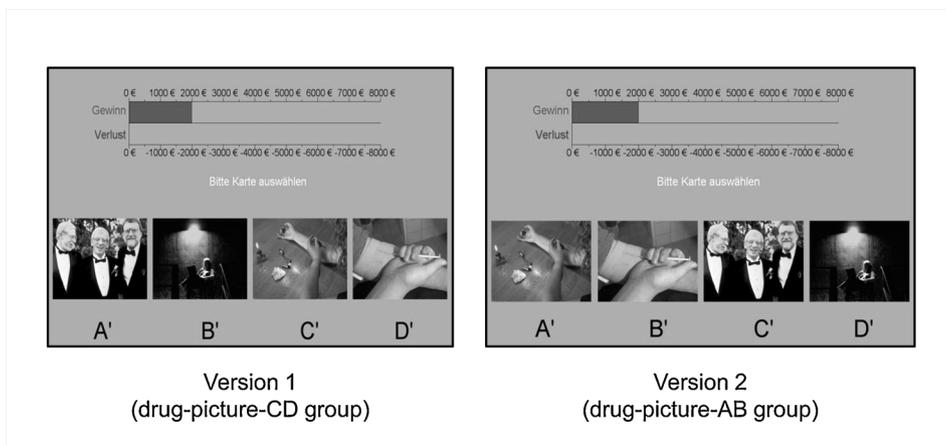


Fig. 1. Modified versions of the IGT. In Version 1, drug-related stimuli are on the advantageous cards stack (drug-picture-CD group) and neutral stimuli are on the disadvantageous cards stack. Version 2 is inverted (drug-picture-AB group).

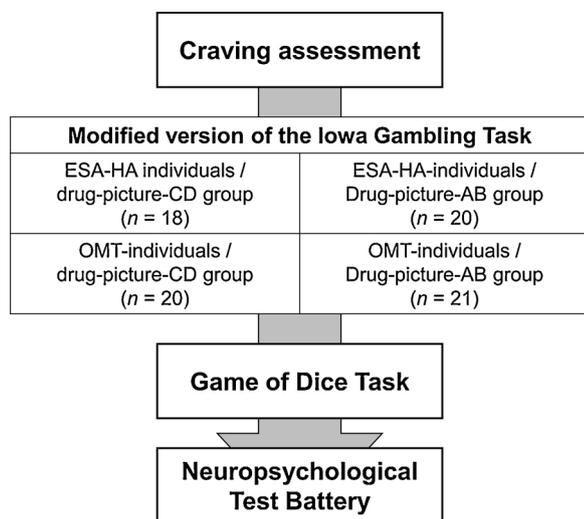


Fig. 2. Procedure of the current study illustrating the 2 × 2 Between Design of the individuals with heroin addiction and the different versions of the IGT.

four numbers) are classified as “low risk”, since the categories have a winning probability of 50% or higher (as done in previous studies, e.g., Brand et al., 2008). The “low risk” categories are associated with low and infrequent losses, the “high risk” categories will lead to frequent and high losses. To evaluate the performance in the GDT, a net score is calculated by subtracting the number of “high risk” decisions from the number of “low risk” decisions. A positive net score displays advantageous decision-making behavior; a negative net score indicates a high-risk behavior. We also used the number of decisions for the riskiest alternative (one single digit).

2.2.4. Neuropsychological test battery

All participants completed a neuropsychological test battery assessing the main cognitive domains with a focus on executive functions. The tests used are listed in Table 2 (for a more detailed description of the tests, see Lezak et al., 2004). The procedure of the current study is shown in Fig. 2.

3. Results

3.1. Results of the craving measurement

To check whether the sight of drug-related stimuli in OMT

individuals triggered less craving than in ESA-HA individuals, the subjectively estimated craving of both groups was compared. Using T-tests for independent samples, the mean values of the two groups are significantly different (ESA-HA individuals $n = 22$, $M = 2.97$, $SD = 2.51$, OMT individuals $M = 1.50$, $SD = 1.12$, $T(25.59) = 3.22$, $p = .015$). Consequently, OMT individuals experience less subjective craving than ESA-HA individuals.

3.2. Results in the modified Iowa Gambling Task (IGTmod)

To check whether OMT individuals showed better performance in the IGTmod than ESA-HA individuals, a two-factorial analysis of variances (ANOVA) was calculated with OMT/ESA-HA group and drug-picture-AB/drug-picture-CD group as between factors and IGT net score as dependent variable. The results indicate a significant main effect for the factor OMT/ESA-HA group, $F(1,79) = 9.14$, $p = .003$, $\eta_p^2 = .073$, as well as the factor drug-picture-AB/drug-picture-CD group, $F(1,79) = 57.97$, $p \leq .001$, $\eta_p^2 = .436$. The interaction was not significant, $F(1,79) = 1.88$, $p = .174$, $\eta_p^2 = .025$. The results are illustrated in Fig. 3. Using the IGT net score of the first block as dependent variable, the results showed no significant main effect of the factor OMT/ESA-HA group, $F(1,79) \leq 0.01$, $p = .964$, $\eta_p^2 \leq .001$ but of the factor drug-picture-AB/drug-picture-CD group, $F(1,79) = 101.98$, $p \leq .001$, $\eta_p^2 = .576$. The interaction was not significant, $F(1,79) = 1.13$, $p = .291$, $\eta_p^2 = .015$. We also calculated a further two-factorial ANOVA with OMT/ESA-HA group and drug-picture-AB/drug-picture-CD group as factors and IGT net score of the fifth block (last 20 trials) as dependent variable showing a main effect of OMT/ESA-HA group, $F(1,79) = 6.67$, $p = .001$, $\eta_p^2 = .082$, a main effect of drug-picture-AB/drug-picture-CD group, $F(1,79) = 12.93$, $p = .001$, $\eta_p^2 = .147$, but no significant interaction, $F(1,79) = 0.11$, $p = .739$, $\eta_p^2 = .001$.

To investigate the performance of the participants in the IGT in more detail, T-tests for independent samples were calculated by comparing the performance of the OMT and ESA-HA individuals. The results illustrate that the OMT/ESA-HA groups do not differ in the IGT overall net score, in the net score of the first block, and of the fifth block in version 1 of the task. In version 2, significant differences in the performance could be observed (see Table 3).

3.3. Results in the Game of Dice Task (GDT)

For analyzing the decision-making behavior under risk between the OMT- and ESA-HA-individuals, T-tests for independent sample were used. The results demonstrate that OMT-individuals showed significantly higher net score, indicating less risky decision-making, than

Table 2
Descriptive values of the neuropsychological paradigms.

| | | Overall Sample M (SD) | OMT-individuals (n = 41) M (SD) | ESA-HA-individuals (n = 38) M (SD) | T | df | p |
|---------------|----------------------|--------------------------|------------------------------------|---------------------------------------|-------|-------|------|
| MCST | Perseverative errors | 2.20 (2.98) | 1.51 (2.14) | 2.89 (3.52) | -2.04 | 72 | .045 |
| ToH | Moves (3 disks) | 15.01 (10.28) | 12.00 (5.91) | 18.29 (12.84) | -2.65 | 46.92 | .011 |
| TMT | Task A (in %) | 51.58 (33.85) | 53.47 (37.91) | 50.53 (31.91) | 0.30 | 51 | .765 |
| | Task B (in %) | 47.38 (36.29) | 50.84 (38.29) | 45.39 (35.53) | 0.52 | 50 | .607 |
| DemTec | Sum Score | 14.39 (3.36) | 14.34 (3.59) | 14.44 (3.11) | -0.13 | 73 | .899 |
| LPS(4) | T-Value | 50.59 (9.20) | 51.34 (9.11) | 49.83 (9.37) | 0.69 | 68 | .495 |

MCST: Modified Card Sorting Test (n = 74), ToH: Tower of Hanoi (n = 73), TMT: Trail Making Test (Task A n = 53, Task B n = 52), DemTec (n = 75), LPS (4): Leistungsprüfungssystem (German intelligence test battery, subtest 4 for logical reasoning n = 70).

ESA-HA-individuals. There were no significant differences regarding the riskiest choice of one number (see Table 4).

4. Discussion

The results showed that in both tasks measuring decision-making behavior, OMT-individuals showed better decision-making performance than ESA-HA-individuals. Investigating decision-making under risk, individuals with long-term treatment showed less risky choices compared to participants at an early stage of complete opioid abstinence. For decision-making under ambiguity, in the first version of the IGT, where the drug-related pictures were presented on the advantageous decks, all participants showed an advantageous decision-making behavior. OMT-individuals performed significantly better than ESA-HA-individuals. In the second version of the IGT, where drug-related pictures were presented on the disadvantageous decks, all the participants performed worse. There were no significant differences regarding both treatment groups. Additionally, it was shown that craving reactions towards drug-related cues were lower in OMT-individuals compared to ESA-HA-individuals. The study may potentially emphasize the efficacy of OMT in heroin addiction for decision-making abilities and craving reactions. It was shown that decision-making behavior was better and craving reactions were lower in the group of individuals receiving maintenance treatment. This is an important aspect, since decision-making impairments and high craving reactions are key factors in the maintenance of drug consumption and can cause high relapse rates (Carter and Tiffany, 1999; Drummond, 2001; Robinson and Berridge, 2008). Former studies mainly outline differences in the decision-making performance between individuals with OUD and

healthy controls (Brand et al., 2008; Lemenager et al., 2011) or between current users and abstinent users (Biernacki et al., 2016). The current results compare different types of treatments and their effects on decision-making behavior. Furthermore, as already mentioned, we investigate the effect of drug-related cues on the decision-making performance. The results of the decision-making behavior in decisions under ambiguity are of high interest. They illustrate that both groups, individuals with OMT as well as individuals at early stage of abstinence, seem to avoid those choice options linked to drug-related cues. This finding is consistent with former research, where individuals with anxiety disorder or substance use disorder showed avoidance behavior in other neuropsychological measurements (Field and Cox, 2008; Heuer et al., 2007; Radke et al., 2013; Rinck and Becker, 2007). Studies investigating the avoidance behavior in OUD using the decision-making task with drug-related stimuli have been missing. The confrontation with specific drug-related cues leads to approach or even avoidance tendencies in individuals with alcohol-use disorder, tobacco use, or cannabis abuse (Cousijn et al., 2012, 2011; Field et al., 2008; Wiers et al., 2013, 2011). The tendency to approach or avoid drug-related cues is associated with cue reactivity and craving. It is described in the multi-dimensional model for alcohol dependency by Breiner et al. (1999). The authors outline the evaluation of the decision for drug consumption. Key mechanisms in this model are, inter alia, different action-tendency states describing the cause of consumption (approach tendency) and the suppression of consumption (avoidance tendency), which depend on positive and negative expectancies towards the drug as well as current and historical factors. In line with dual-process approaches, it is assumed that there is an imbalance between automatic and controlled processes (Bechara, 2005; Wiers and Stacy, 2006).

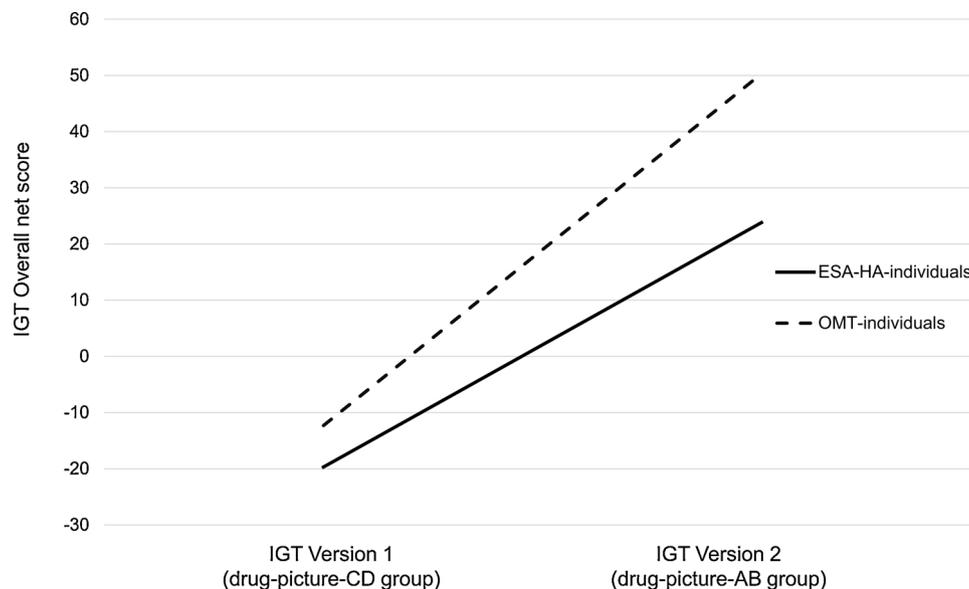


Fig. 3. Results of the performance in the IGT.

Table 3
Group comparison of the performance in the modified IGT.

| | | Overall Sample <i>M (SD)</i> | OMT-individuals (<i>n</i> = 41) <i>M (SD)</i> | ESA-HA-individuals (<i>n</i> = 38) <i>M (SD)</i> | <i>T</i> | <i>df</i> | <i>p</i> |
|--|----------------------------------|---------------------------------|---|--|----------|-----------|----------|
| drug-picture-CD group <i>n</i> = 38 | Overall net score | −15.79 (35.87) | −12.30 (33.65) | −19.67 (38.80) | 0.63 | 36 | .535 |
| | Net score Block 1 (round 1-20) | −11.58 (7.60) | 22.95(10.97) | 27.39 (10.08) | −1.29 | 36 | .204 |
| | Net score Block 5 (round 81-100) | 8.63 (9.80) | 24.70 (12.80) | 21.28 (10.68) | 0.89 | 36 | .380 |
| drug-picture-AB group <i>n</i> = 41 | Overall net score | 37.37 (28.15) | 50.29 (13.75) | 23.80 (33.04) | 3.32 | 25.13 | .003 |
| | Net score Block 1 (round 1-20) | 9.90 (10.71) | 11.29 (4.43) | 16.65 (7.88) | −2.67 | 29.62 | .012 |
| | Net score Block 5 (round 81-100) | −0.10 (12.07) | 39.52 (1.75) | 31.50 (8.29) | 4.24 | 20.61 | ≤ .001 |

Table 4
Group comparison of the performance in the GDT.

| | Overall Sample <i>M (SD)</i> | OMT-individuals (<i>n</i> = 39) <i>M (SD)</i> | ESA-HA-individuals (<i>n</i> = 35) <i>M (SD)</i> | <i>T</i> | <i>df</i> | <i>p</i> |
|-------------------------------------|---------------------------------|---|--|----------|-----------|----------|
| GDT net score | 4.43 (11.18) | 8.21 (10.02) | 0.23 (11.04) | 3.26 | 72 | .002 |
| GDT number of riskiest alternatives | 2.57 (3.53) | 2.23 (3.04) | 2.94 (4.01) | −0.87 | 72 | .390 |

Bechara (2005) outlines that these two neural processes are affected by addictive behaviors. The impulsive system, associated with the amygdala, reacts to immediate rewards and punishments. The reflective system, associated with the dorsolateral prefrontal cortex, supports the consideration of long-term consequences. It is assumed that the dominance of an impulsive system induces approach tendencies such as to consume a drug. Avoidance tendencies, such as to suppress the urge of consumption, are related to the activation of the reflective system (Wiers and Stacy, 2006). Regarding the current results, we must keep in mind that the OMT-individuals are in a long-term treatment. They may potentially learn to control their drug-related urges and drives and to avoid situations that are related to previous drug intake. This could lead to a cognitive control over the impulsive reaction demonstrated by the avoidance of drug-related cues even if it results in disadvantageous decisions in the IGT. Additionally, individuals in an earlier stage of abstinence also showed avoidance tendencies. These tendencies were not as high as in individuals who experienced a long-term treatment. Furthermore, the reduced craving reactions emphasize the argument that the reflective system affects decision-making behavior even if dysfunctional and impulsive tendencies have been built before (see also Snagowski and Brand, 2015). The review about the understanding of OUD by Moninka et al. (2019) also outlines the interplay of affective and cognitive components, difficulties in emotion/stress regulation, as well as impairments in cognitive functions. The current results are a first hint, which emphasize this interplay of cognitive components such as the decision-making performance and affective components such as the salience of drug-related cues. However, we could not specify the causality of craving and decision-making capabilities, which seem to be of high relevance and should be addressed in future studies.

Some limitations have to be mentioned. Decision-making behavior of individuals with current heroin addiction is difficult to investigate. First, heroin use on the day of investigation might affect the performance due to the sedating and psychotropic effects of heroin. Second, the requirement of heroin abstinence at the day of investigation could lead to withdrawal symptoms, which might as well affect the decision-making performance, e.g., continuous attention on the task. Therefore, individuals with heroin addiction at the end of an inpatient detoxification treatment seemed to be the fit best for investigating the group of ESA-HA-individuals without the confounding effects of heroin intoxication and withdrawal (see also Brand et al., 2008). Furthermore, for the OMT-group, we defined a comorbid alcohol dependence or further current drug abuse as additional exclusion criteria to investigate the relevance of OMT as controlled as possible. However, we are aware that this is a high-functioning group of OMT-individuals. The effects of the comparison between individuals with and without OMT cannot be

generalized to those individuals with OMT and further comorbid drug abuse automatically. Additionally, further information regarding the time of detoxification, the medication in the control group, or the dose of medication are missing. We know that this could have an effect on the results and could be important for understanding the relevance length of OMT or abstinence or even the changes of cognitive functions. We highly recommend further research to keep this in mind and also to control for the relevance of OMT and cognitive functioning with multiple drug abuse. One further limitation is the differences between the groups in some demographic variables such as age, injection phobia, and intravenous drug abuse. Age especially should be taken into consideration, since this could affect the performance in the decision-making tasks. However, previous research identified that older participants show higher impairments in both tasks compared to younger individuals (Schiebener and Brand, 2015). The relevance of injection phobia and intravenous drug abuse should be considered in further studies; nonetheless, we do not expect changes of the main effects, since for example only five participants in total showed this form of phobia.

To our knowledge, this is the first study investigating the interplay of decision-making and additional confrontation with drug-related cues in OMT-individuals in comparison to ESA-HA-individuals. One well-proven effect of OMT is the marked reduction of heroin use in up to 70–80% of individuals in continuous treatment (Wittchen et al., 2008). This effect is attributed to the suppression of withdrawal symptoms and withdrawal-induced heroin craving by the administration of a long-acting opioid such as methadone. Potentially due to long-term suppression of heroin intake, the decision-making of OMT-individuals improves, thereby lowering the risk of renewed heroin use as far as OMT is continued (Sees et al., 2000). However, it should be considered that long-term OMT-individuals with a mean duration of OMT of more than eight years are a highly selected group of individuals with heroin addiction, given retention rates of 60–70% per year in OMT in routine care in Germany (Wittchen et al., 2008). Prospective longitudinal studies should investigate if the long-term participation in OMT is a result of a less impaired decision-making already at the start of OMT or whether decision-making improves over the course of OMT. Such long-term studies should additionally clarify the different mechanisms underlying the decision-making behavior. It could be assumed that the reduction of craving affects the decision-making behavior and supports the reflective system to avoid drug-related situations. In addition, the relevance of cognitive control as an important factor in long-term treatment is reflected by the ability to make less risky decisions. This interplay of different processes, for example as the potential interaction of cue reactivity and craving with executive functions, and decision-making behavior in different situations, could be a good starting point

for a better understanding of treatment efficacy. Nevertheless, there is evidence that in a long-term course of heroin addiction, individuals often change between states of in treatment versus out of treatment (Scherbaum and Specka, 2008), which could also reflect decision-making guided more strongly by the impulsive versus reflective system.

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Contributors

JK and SW collected the data, and JK, MB, and EW conducted the statistical analysis and interpreted the results. JK, MB, NS, and EW conceptualized and wrote the first draft of the manuscript. SW and FR aided in data collection, data interpretation, and writing the manuscript. NS designed the study and supervised together with EW interpreting the data and writing the manuscript. All authors contributed to and have approved the final manuscript.

All other authors declare no conflict of interest.

Declaration of Competing Interest

Prof. Dr. N. Scherbaum received honoraria for several activities (advisory boards, lectures, manuscripts) by the factories AbbVie, MSD, Medice, Reckitt-Benckiser/Indivior, and Sanofi-Aventis. During the last three years, he participated in clinical trials financed by the pharmaceutical industry.

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