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Methadone maintenance treatment patients with a history of childhood trauma succeed more in a cognitive paradigm that is associated with a negative reward

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ABSTRACT

Previously we showed that methadone maintenance treatment (MMT) patients displayed difficulties in generalization and reversal learning in the presence of drug-related context, compared to prolonged abstinence individuals. We now tested how history of childhood trauma, affects their reversal learning abilities. Fifty-one MMT patients were evaluated on a performance- based paradigm which assesses the ability to acquire and reverse stimulus–outcome associations in neutral and drug-related context. Patients with a history of childhood trauma (n = 32) as compared to patients without such a history showed decreased ability to learn associations with positive outcome, and had poorer performance in drug compare to neutral-related context. Most importantly, while individuals with childhood trauma history showed higher success rates in conditions of positive to negative reversals, an opposite pattern was observed in conditions of negative to positive reversal; whereas patients with trauma history preformed significantly worse than patients with no history. The results are in line with other studies which tested the effects of childhood trauma both in clinical and in healthy populations. Recognizing this trait that more disturbed by drug related context, may contribute to develop and improve personalized treatments which takes into account the difficulties as well as the strength associated with childhood trauma.

1. Introduction

Substance use disorder is a chronic relapsing brain disorder (Koob and Volkow, 2010). The frequency of relapses as well as the frequency of withdrawal and craving symptoms are augmented in the presence of contextual reminders, such as places, persons, and articles linked to drug use (O'Brien et al., 1998; Tifany, 1990). Conditioning and learning processes are created during drug use, yet remain intact even after long abstinence (O'Brien et al., 1998). Substance use disorder produces its rewarding effects by increase dopamine neurotransmission in the mesolimbic system (Wise, 2004). In opioid use disorder, the dopamine increase is results of GABA disinhibition that mediated by opioids when bind the mu opioid receptors (Johnson and North, 1992). For opioid use disorder, there is chronic treatment namely maintenance with long-acting opioid mu receptor agonists, such as methadone or buprenorphine, and is the most effective treatment for most individuals with opioid use disorder (Mattick et al., 2014). Individuals with opioid use disorder that already receiving methadone maintenance treatment (MMT) also presented in a case-control study a faster respond to pictures of drug-related context compared to pictures of neutral context than a healthy controls (Lubman et al., 2000). The phenomena associated with relapses are related to a flawed reversal learning capability (i.e., the inability to learn that stimuli associated with a positive outcome may have a negative outcome when presented in a different context), as was shown in patients with alcohol use disorder (Máttyássy et al., 2012; Rustemeier et al., 2012) and cocaine use disorder (Camchong et al., 2011). In a previous study we compared individuals with opioid use disorder who weaned themselves off opioids and stayed drug-free for at least 10 years to a group of patients with similar characteristics who were in MMT for at least 10 years (Levy-Gigi et al., 2014). The groups were comparable in all task performances with one exception: unlike prolonged abstinence individuals, the group of patients receiving MMT failed to successfully perform a specific reversal learning task (when a positive stimulus becomes negative) in the

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Table 1
Characteristics of study patients, and comparison between the two study groups.

	All patients	History of childhood-trauma	No history of childhood trauma	*p* value (*F*)
N (%)	51 (100)	32 (100)	19 (100)	
Female sex	18 (35.3)	16 (50.0)	2 (10.5)	0.006
Age * (years)	51.7 ± 1.2	49.2 ± 1.4	56 ± 2.1	0.008 (7.8)
Years of education *€	9.5 ± 0.4	9.5 ± 0.5	9.7 ± 0.6	0.8
Lifetime history of self-harm	21 (41.2)	17(53.1)	4(21.1)	0.04
Suicide attempt	14 (27.5)	10 (31.3)	4 (21.1)	0.5
Other self-harm ‡	13 (25.5)	12 (37.5)	1 (5.3)	0.02
Positive drugs in urine test ≠	19 (37.3)	13(40.6)	6 (31.6)	0.6
Cocaine	9 (17.6)	6 (18.8)	3 (15.8)	1
Cannabis	2 (3.9)	2 (6.3)	0 (0)	0.5
Benzodiazepines	9 (17.6)	6 (18.8)	3 (15.8)	1
Opioids	8 (15.7)	7 (21.9)	1 (5.3)	0.2
Age at opiates use onset *	20 ± 0.8	19.8 ± 1.0	21.5 ± 1.2	0.3
Duration of opiates use * π (years)	18.8 ± 1.5	17.5 ± 1.8	21.1 ± 2.7	0.3
Ever intravenous injection £	30 (62.5)	11 (36.7)	7 (38.9)	1
Age started MMT * (years)	39.3 ± 1.4	37.3 ± 1.6	42.6 ± 2.3	0.06
Duration in MMT * (years)	9.1 ± 1.1	8.0 ± 1.3	11.0 ± 2.0	0.2
Methadone current dosage * (mg/day)	122.5 ± 6.3	119.3 ± 8.3	127.6 ± 9.8	0.5

Chi square or Fisher's exact test. *Mean ± SE, ANOVA.
MMT, methadone maintenance treatment.
€ years of education includes elementary school (8 years), high school (4 years) and university.
‡ Other self harm - self-ignition, self damage.
≠ positive drugs in urine was defined according to the results of all the urine drug screenings in the month preceding the computerized. assignment, being positive if at least one tests was positive; urine could be positive for more than one drug.
π defined by the difference between the age at opiates use onset (as reported by each patient) and the age starting MMT.
£ information was taken from patients' records that include modified Addiction Severity Index (McLellan et al., 1984).

presence of drug-related contextual reminders.

Specifically, we found (Levy-Gigi et al., 2014) that both groups could link a stimulus to either a positive or a negative outcome, whether the stimulus' context was neutral or drug-related. Furthermore, both groups succeeded in reconditioning the reversed stimulus (i.e., a positive outcome that became negative or a negative outcome that became positive) in a neutral context. In addition, there was no difference between the two groups when we examined reconditioning of a stimulus with a negative outcome that became a positive outcome in a drug-related context. Nevertheless, when we tested a stimulus with a positive outcome that became negative in a drug-related context, patients receiving MMT showed significantly lower success rates when compared to the prolonged abstinence individuals. This could interpreted that once individuals with substance use disorder linked a certain stimulus in a drug-related context with a positive outcome, they failed to link that same stimulus with a negative outcome. Such a difficulty was demonstrated in alcohol use disorder patients (Máttyássy et al., 2012). Still, this finding was demonstrated in a small homogenous group that was compared with a rare individuals who succeeded prolonged abstinence. It was important to further expand the research to a more heterogeneous group of MMT patients.

In the current study, we examined how both the stimulus' valence (positive reward versus a negative reward) and the context in which the stimulus was presented (neutral image versus drug-related image) affect the ability to recondition previously acquired information. We were specifically interested in patients a with history of childhood traumas, which is highly prevalent among patients receiving MMT (Engstrom et al., 2012; Vogel et al., 2011), and variable that was not included in our previous study (Levy-Gigi et al., 2014). Such individuals had been reported to pay greater attention to negative stimuli and rewards than to positive ones (Rozin and Royzman, 2001). Given the impaired ability that was documented in a group of patients receiving MMT to reverse a positive stimulus into a negative outcome (Levy-Gigi et al., 2014), we also studied the two different effects in that group.

2. Methods

This study was approved by the Tel Aviv Sourasky Medical Center Institutional Review Board Helsinki committee.

2.1. Study population

Patients in the Adelson MMT Clinic in Sourasky Medical Center, Tel-Aviv, Israel comprised the study cohort. The clinic treats patients who meet the DSM-IV-TR criteria for opioid dependence. Inclusions were patients who were in treatment for at least 3 months, and signed inform consent

2.2. Study process

Out of the 63 patients who met the study inclusion criteria and were asked to participate in the study, 51 (81% compliance) agreed, eight refused at the outset, and four refused to finish the computerized assignment. The 51 enrolled patients were administered their usual current methadone daily treatment medication in the morning, signed a consent form, and performed the computerized assignment (see Section 2.4 below) following 9.8 ± 9.4 minutes, before reaching the peak methadone effect at 2–4 hours (Rass et al., 2014). Treatment information (methadone current dose, urine results), sociodemographic and variables related to their addiction history and lifetime history of adverse events were taken from patients' records that include modified Addiction Severity Index (McLellan et al. 1984), self-report questionnaires about their lifetime history of adverse events traumas or abuse during childhood (physical and verbal abuse, sexual abuse or rape) (Rowan et al., 1994), and of attempted self-harm (suicide attempt, self-ignition or other forms of self-harm).

2.3. Drugs in urine

Our patients receiving MMT are routinely screened for drugs in their urine in a random observed manner at least twice each month. Urine is tested for the presence of opioids, cocaine metabolite (benzoylecgonine), benzodiazepines, cannabis, and amphetamines by means of the Enzyme Immunoassay systems DRI and CEDIA (Hawks, 1987). The results in the month preceding the computerized assignment were taken for the study analyses, and were defined as being positive if at least one

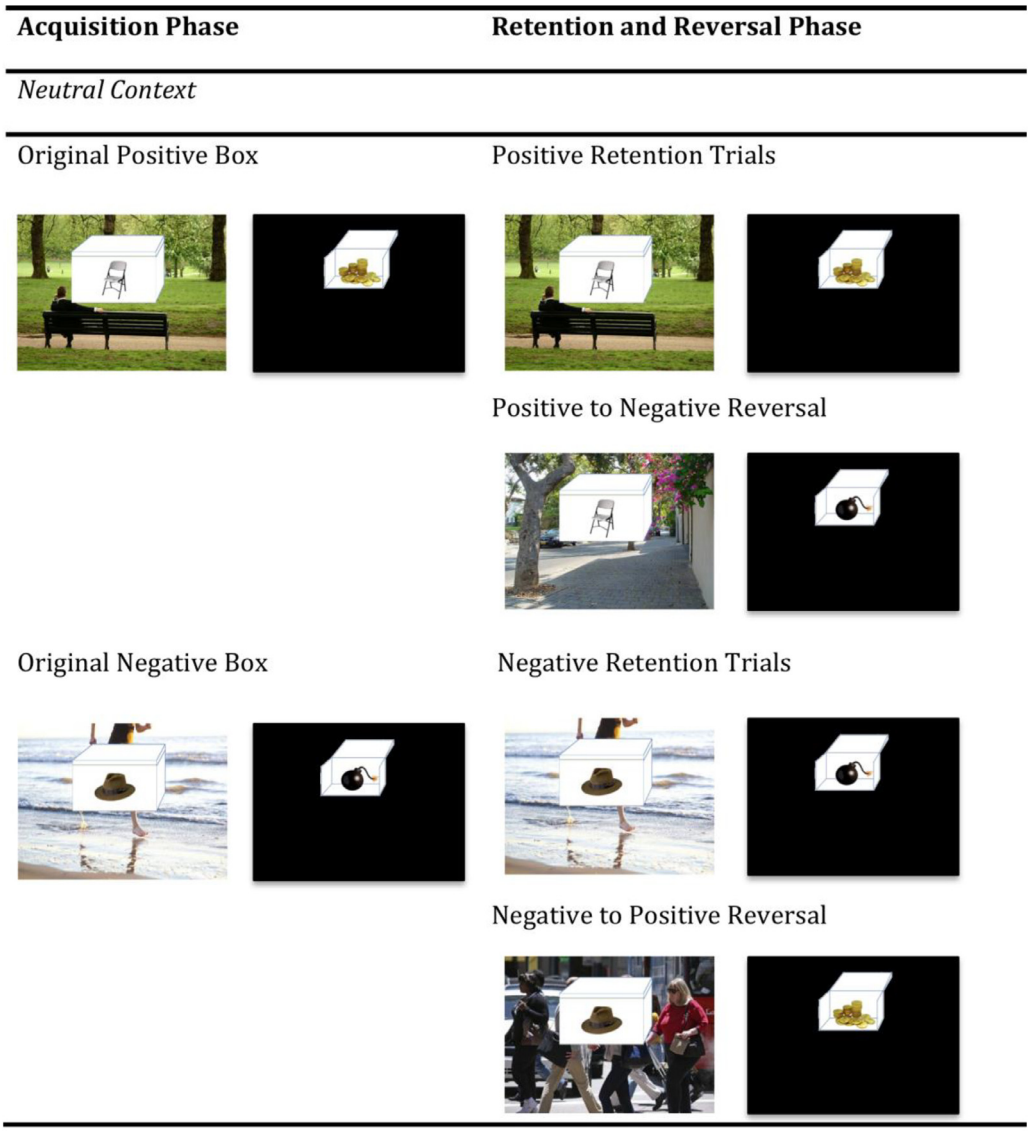

Fig. 1. Screen shots from the object stimulus-background context reversal paradigm, demonstrating a positive stimulus and a negative stimulus that are presented in a neutral context during all of the 3 assignment's phases. During the reversal phase, same stimulus as in the previous phases is shown (in this figure, a chair and a hat), but with a different neutral context background. The stimulus' outcome in this phase is also changed from positive to negative, or vice versa. Patients are expected to recondition the firstly acquired stimulus to the opposite type (i.e. perform reversal learning), as reflected in the background image context replacement.

tests was positive. The use of each substance separately is presented in Table 1. However, due to small sample numbers and based on our previews studies (i.e. Elkana et al., 2017) we grouped all users into one group.

2.4. Stimulus-context reversal paradigm

The paradigm is described in detail by Levy-Gigi et al. (2014). In brief, the patient is shown boxes with an illustration of an everyday object, such as a chair or a car. That object represents the stimulus. Each box is presented against a background image, which could be neutral (Fig. 1) or have a drug-related context (Fig. 2). The patient chooses whether to open the box or leave it closed. The patient's goal is to open all the boxes that hold a positive outcome (money) and leave the boxes linked with a negative outcome closed (bomb) (Fig. 3).

Fixed combinations of objects and background images are presented in the first phase of the paradigm, the acquisition phase. Patients need to reach the objective of six consecutive correct responses within a minimum of 40 acquisition trials. Patients who succeed in doing so can proceed automatically to the next phase. Patients who fail receive additional trials (two sets of 12 trials), and those who do not reach the objective within the maximum 64 trials are dropped from the task. In the next phase, the same combinations from the acquisition phase are shown to the patient (retention trials), together with new combinations in which old boxes are presented against a new background (neutral or drug-related). In addition to the change in the background image, the reward inside the box is also reversed: a box containing a positive reward will now contain a negative one, and vice versa. This phase tests reversal learning ability (see Figs. 1 and 2 for neutral and drug related context conditions respectively).

The patient is expected to conclude that even though the box shows the same object (i.e., the same stimulus), the change in the background image is accompanied with a reversal of the outcome of the box. In the reversal trials, the patients need to learn that a stimulus that was initially linked with a certain outcome can now be associated with a different one. For example, in the first part of the paradigm, a box with an illustration of a chair is shown on the background of a park. This combination is always linked to a positive reward, and the patient is

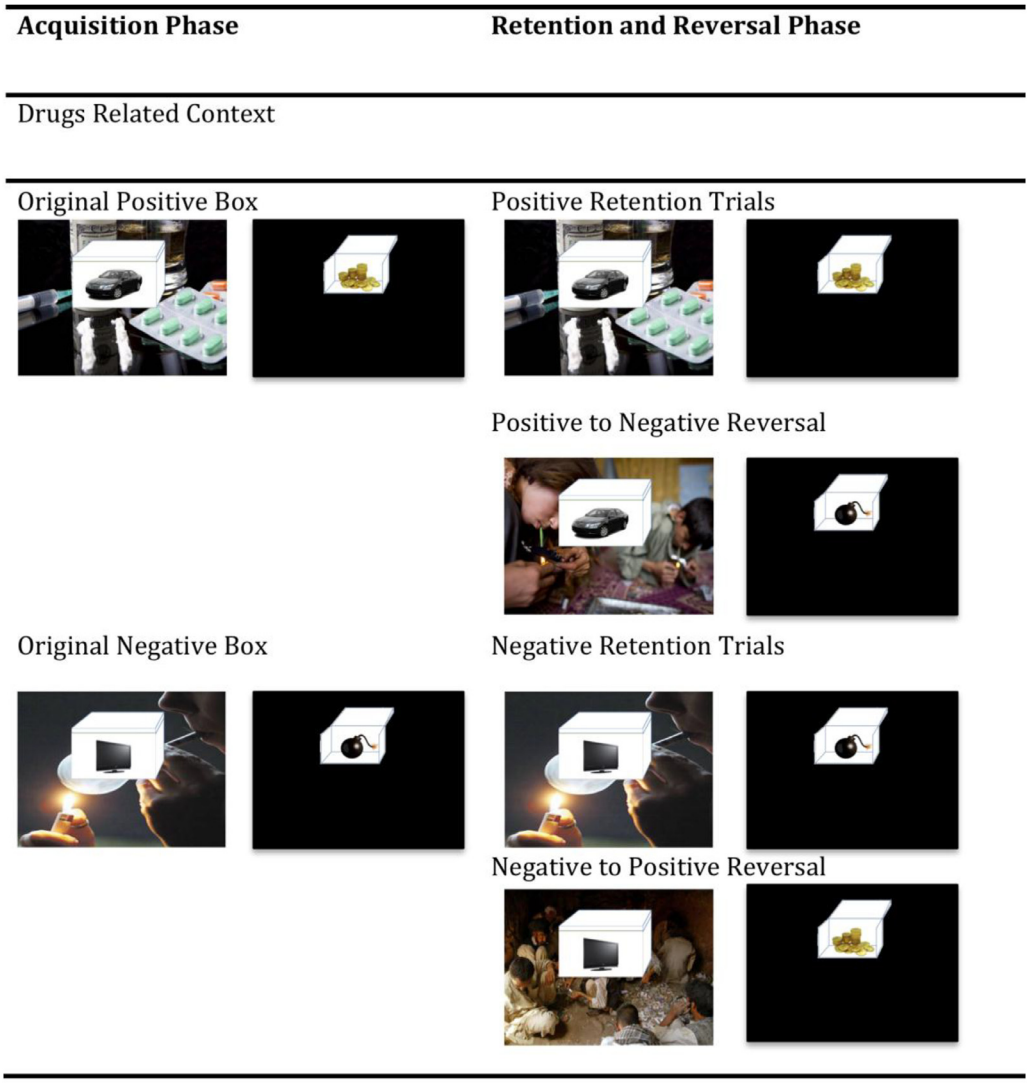

Fig. 2. Screen shots from the object stimulus-background context reversal paradigm, demonstrating a positive stimulus and a negative stimulus that are presented in a drug-related context during all of the 3 assignment's phases. During the reversal phase, same stimulus as in the previous phases is shown (in this figure, a car and a television), but with a different drug-related context background. The stimulus' outcome in this phase is also changed from positive to negative, or vice versa. Patients are expected to recondition the firstly acquired stimulus to the opposite type (i.e. perform reversal learning), as reflected in the background image context replacement.

expected to open such boxes. In the second part, a new box showing the same chair is presented over a background of a busy street. This new combination always leads to a negative reward, and after several trials and errors, the patient is expected to leave such boxes closed, but they are still expected to open boxes that show the chair-park combination that contains a positive reward.

The proportions of correct answers given to different contexts and outcomes were calculated and used in the analyses, comparing each phase of the assignment (acquisition, retention, and reversal) individually, and the relationships between the variables for each phase independently and for several phases combined.

2.5. Data analysis

We used SPSS (version 22) software (SPSS Inc., Chicago, IL) to analyze the data. The Chi-square test and the Fisher's exact test were used for categorical variables and the analyses of variance (ANOVAs) were used for continuous variables. Mean and standard error values are shown in the Results section below. In order to test the performance in the computerized assignment and for comparing between groups' performance level, we used the repeated measure test, considering the assignment's phase (acquisition or retention), valence (positive or negative reward) and context (neutral or drug-related). Mean and standard error (SE) values are presented when both groups are compared.

3. Results

3.1. Characteristics of study group

Table 1 depicts the characteristics of the study group. Fifty-one patients comprised of 18 (35.3%) females and 33 (64.7%) males, with mean age of 51.7 ± 1.2 years, comprised the study cohort. They had a history of 18.8 ± 1.5 years of opioid use (43.1% for ≥20 years), and 30 (62.5%) of them had administrated substance intravenously at least once. Their mean duration in MMT was 9.1 ± 1.1 years, and their current daily methadone dose was 122.5 ± 6.3 mg/day. Positive results of any substance in urine were detected among 19 (37.3%) of them (detailed results of each substance is presented in Table 1). Thirty-two patients (62.7%) reported on lifetime history of childhood traumas: 27 were physically abused and 12 were raped or sexually abused. The group with a history of childhood trauma had a higher proportion of females ($p = .006$), was younger on average ($p = .008$), and more of them had a history of self-harm other than suicide attempt ($p = .04$) (Table 1).

3.2. Task performance

Task performance was not significantly related to clinical treatment variables (methadone dosage and duration in MMT), current substance use, sociodemographic variables including years of education, as well

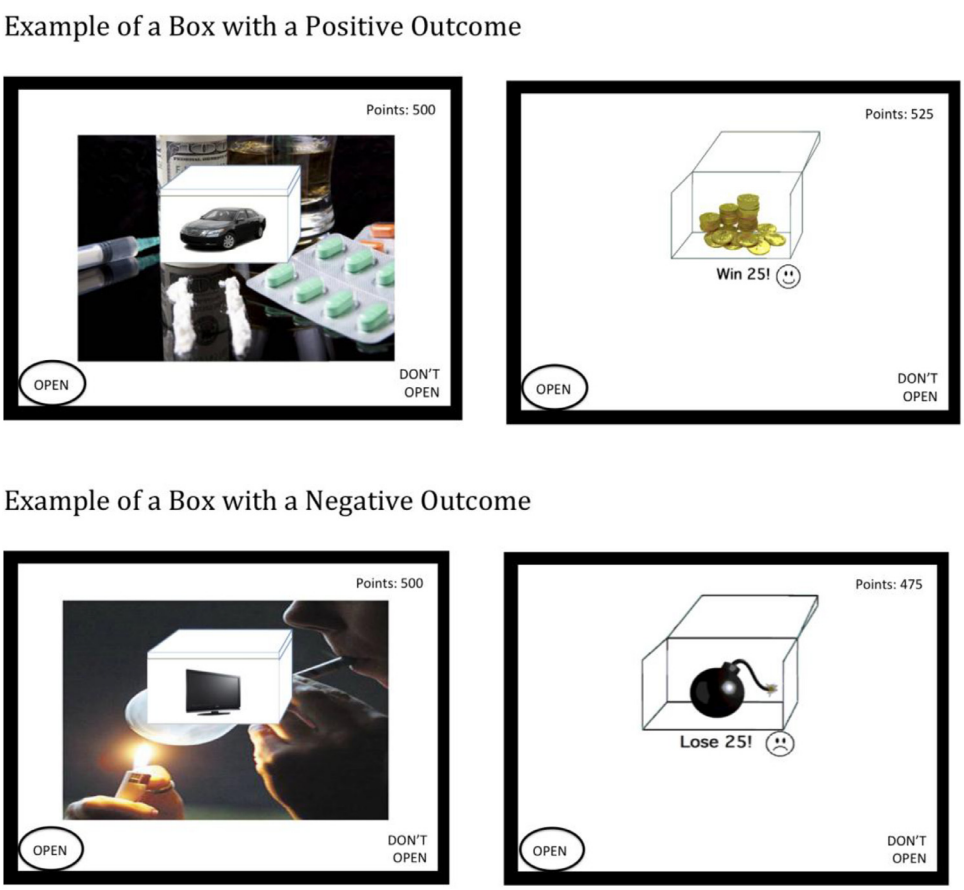

Fig. 3. Screen shots from the object stimulus-background context reversal paradigm, showing examples of stimuli with a positive and a negative outcome (here presented over a drug-related context). Patient may choose to open a box, accepting whatever reward is inside of it, or leave the box closed.

as the variables that significantly differed between study groups (sex, age, and percentage of history of self-harm) (data are not shown).

3.3. History of childhood trauma and conditional learning

3.3.1. Acquisition and retention of stimulus-outcome associations

We conducted repeated measures ANOVAs to compare the stimulus' valance (positive versus negative) and context (neutral versus drug-related) for acquisition and retention trials using childhood trauma as the between-subject factor. The results revealed that patients with childhood traumas displayed an overall poorer ability to acquire stimulus-outcome associations compared to patients with no childhood traumas (65.7 ± 2.8 and 75.9 ± 3.6, respectively, F (1,49) = 5.11, p = .03, $\eta 2$ = .09). However, both groups performed similarly in the retention phase, (58.7 ± 2.0 and 58.5 ± 2.5, respectively, F (1,49) = .004, p = .95). These results indicate that while having a history of childhood trauma may impair the pace of acquisition, the ability to retain it remains intact as soon as the material is learned. In addition we found significant interaction between the stimulus' valance and a history of childhood trauma (F(1,49) = 4.24, p = .04, $\eta 2$ = .08): A follow-up pairwise comparison revealed that while there were no significant differences between the groups in acquiring negative stimulus outcome associations (77.8 ± 3.2 versus 78.3 ± 5.6 respectively, t(1,49) = 0.08, p = .9), individuals with a history of childhood trauma were significantly worse in acquiring positive stimulus outcome associations compared to individuals with no history of childhood trauma (53.6 ± 4.2 and 73.5 ± 5.7, respectively, t(1,49) = 2.8, p = .007, see Fig. 4). In addition, we found a significant interaction between the stimulus' context and a history of childhood trauma (F (1,49) = 4.49, p < .04, $\eta 2$ = .08). A follow-up pairwise comparison

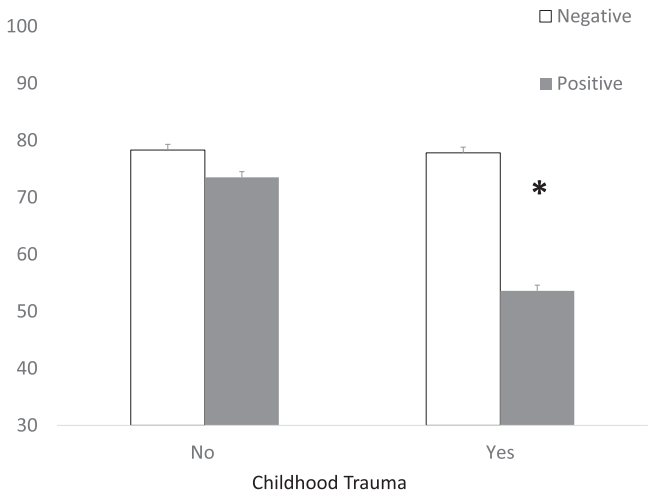

Fig. 4. The success rate of acquisition phase by stimulus' valence (positive versus negative) and by a history of childhood trauma. Percentage of correct answers in the acquisition phase by stimulus' valence (positive versus negative) as influenced by a history of childhood trauma. Both groups did similarly well in acquiring negative stimulus outcome associations (white columns, p = .9), patients with a history of childhood trauma were significantly worse in acquiring positive stimulus outcome associations (grey columns, p = .007).

revealed that while both groups acquired neutral context stimulus-outcome associations equally well (70.3 ± 3.3 and 73.2 ± 5.2, respectively, t(1,49) = 0.5, p = .6), patients with a history of childhood trauma performed significantly worse when the stimuli were presented in a drug-related context compared to patients without such history

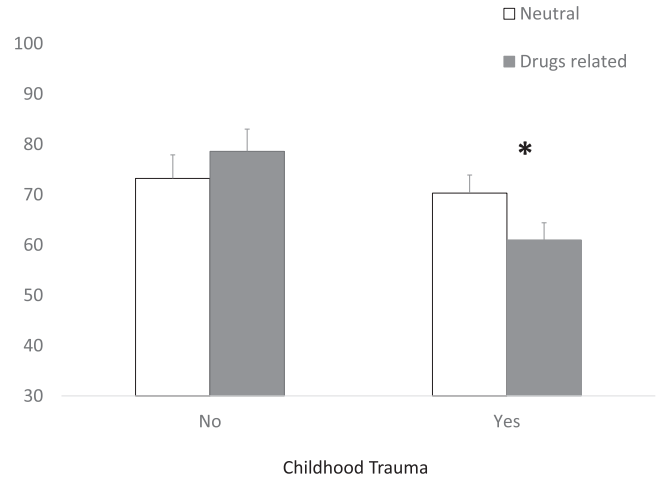

Fig. 5. The success rate of acquisition phase by stimulus' context (neutral versus drugs related) and by a history of childhood trauma. Percentage of correct answers in the acquisition phase by stimulus' context (neutral versus drugs related) computerized assignment, as influenced by a history of childhood trauma. There were no significant differences between the two groups in acquiring stimuli presented in a neutral context (white columns, $p = .6$); however patients with a history of childhood trauma were significantly worse in acquiring stimuli presented in a drug-related context (grey columns, $p = .002$).

(61.0 ± 3.2 and 78.6 ± 4.5, respectively, $t(1,49) = 3.2$, $p = .002$, see Fig. 5).

3.3.2. *Reversal learning*

In order to compare the performance on the reversal trials we conducted a repeated measures ANOVA with context (neutral vs. drugs related), reversal type (object stimulus vs. background context) and reversal valance (from positive to negative vs. from negative to positive) as the within-subject factors and a history of childhood trauma (no vs. yes) as the between subjects factor. The results revealed a significant interaction between reversal valance and a history of childhood trauma ($F(1,49) = 4.66$, $p < .04$, $\eta 2 = .09$). Follow-up pairwise comparisons revealed that while in the positive to negative reversal condition individuals with a history of childhood trauma performed better than individuals with no trauma ($t(49) = -2.07$, $p < .05$), in negative to positive conditions individuals with no history of childhood trauma performed better than individuals with a history of childhood trauma ($t(49) = -2.14$, $p < .04$). There were no significant differences in the performance of the groups as a function of context and reversal type. Hence individuals with and without a history of childhood trauma were equally able to reverse neutral and drugs related stimulus-outcome associations as well as stimuli and context related information.

4. Discussion

The objective of this work was to analyze the difference in reversal learning abilities between MMT patients with a history of childhood traumas to those without. The results revealed that patients with a history of childhood trauma had difficulties in acquiring outcome with no difference in retaining stimuli from the patients with no history of trauma. Specifically, the difficulties in acquisition was related with a positive outcome and with drug related context. In the reversal learning phase, patients with a history of childhood trauma performed better in reversing a positive stimulus to a negative one than those with no childhood trauma, while the opposite namely reversing a negative stimulus to a positive one was performed better among patients with no childhood trauma.

We previously found (Levy-Gigi et al., 2014) that MMT patients had difficulty in reversing a stimulus with a positive reward to a negative reward in a drug-related context. The current study extends and deepen our investigation by assessing the ability to acquire, retain and reverse stimulus-outcome associations as a function of a history of childhood trauma. Specifically, in the acquisition phase and the retention phase, each requiring basic cognitive functions such as visual perception and memory, as well as in the third phase (reversal) which is more complex, and requires flexible thinking (the ability to change and reverse an existing association), which is a component of high cognitive executive functioning.

Interestingly, while they had no difficulties in the application of positive to negative reversals, patients with a history of childhood trauma had difficulty in reversing a stimulus with a negative reward to a positive one. They also performed better in learning stimuli that led to a negative reward compared to stimuli with a positive reward. This phenomenon is supported by a model according to which stimuli with a negative valence have a more significant impact than similar stimuli with a positive valence (trait-negativity bias), and the tendency of negative events, information, or feedback to more profoundly affect feelings, thoughts, decisions, and behavior (Rozin and Royzman, 2001). Negative contents have a considerable influence on the formation of impressions, and negative information receives more processing resources and is superior to establishing an impression about a certain stimulus compared to positive information (Anderson, 1965; Skowronski and Carlston, 1989). Studies on learning processes have consistently shown that punishment or negative rewards given for wrong answers are more influential and lead to faster learning (Baumeister et al., 2001; Meyer and Offenbach, 1961). Moreover, events that prompted fear or terror leave their mark years later, and the brain's activity pattern in response to the stimulus remains as it was even after the behavioral response to a fear-inducing stimulus has faded (Quirk et al., 1995). Vythilingam et al. (2007) showed that PTSD victims demonstrated higher sensitivity and attention to negative or threatening stimuli as opposed to positive stimuli compared to healthy controls. Another study (Fani et al., 2012) confirmed those results, and added that PTSD victims strain to eradicate conditionings linked with fear and horror. On the other hand, trauma victims who do not suffer from PTSD tend not to exhibit such a pattern of behavior. A third study (Constans, 2005), found that even stimuli which are unrelated to trauma, when experienced by PTSD victims, lead to similar results of preferring negative over positive, and therefore this thought pattern is common to all trauma victims, and not only to PTSD victims.

Patients with depressive disorder also tend to have similar thought patterns (Beck, 1987; Elliott et al., 1996; Shook et al., 2007). Apart from preferring the negative properties of events and experiences over positive ones, they tend to give a negative, aggravated interpretation to neutral and even positive events. Additionally, while people who do not suffer from depressive disorder succeed in breaking the negative stigma when given repeated positive feedbacks (i.e., they succeed in negative to positive reversal), patients with depressive disorder are locked in a hopelessness perception and are unwilling to change (Beck, 1987; Elliott et al., 1996; Shook et al., 2007). Likewise, patients with anxiety disorders and dysphoria who do not suffer from depression show an inclination towards negative information (Bradley et al., 1997). Anxiety disorders can result from childhood trauma. Bradley et al. (1997) suggested that even if at first patients with depressive and anxiety disorder automatically notice negative stimuli, once their attention had been gained, they will not be able to remove it from the negative stimulus, and maybe even go on to perform a negative to positive reversal.

Aas et al. (2017) conducted a study on patients with psychiatric disorders who suffered from childhood abuse and found a link between the severity of the abuse, the emotional response, and brain activity. Their results showed that negative stimuli resulted in higher levels of response which, in turn, correlated with more severe abuse. Those researchers hypothesized that patients with a history of childhood trauma devote more attention to negative stimuli than to positive stimuli.

Interestingly, many studies found that positive reinforcement is a better contributor for behavioral change and drug abstinence among

individuals with drug use disorder, a process known as contingency management. Many studies have demonstrated the efficacy of positive reinforcement in extending abstinence duration among MMT patients (Higgins and Silverman, 1999; Kidorf and Stitzer, 1999; Silverman et al., 1998). One study showed that as the reinforcement value increases, so does the chance that patients receiving MMT will avoid using opioids and other drugs during therapy (Dallery et al., 2001). Although never stand alone, this raise a question to what extent contingency management influences patients with a history of childhood trauma who manage to learn mainly from negative rewards. A study that examined the relationship between PTSD symptoms and contingency management therapy found that complex PTSD reduces the efficacy of therapy (Herman, 1992). However, factors such as a history of trauma, the severity of psychiatric comorbidities, psychological stressors, and complex PTSD symptoms did not have a significant influence on the efficacy of therapy (Ford et al., 2007; Weinstock et al., 2007). It would be of interest to study whether the success rates in our study's computerized assignment be related or affected as a result of contingency management therapy. Interestingly, a study held among homeless cocaine abusers showed that patients with PTSD had higher abstinence rates during contingency management therapy compared with patients without PTSD (Burns et al., 2010). Lastly, it seems that traumatic past events intensify learning of negative experiences (over positive experience), but the connection between learning abilities and contingency management therapy remains unclear.

Patients with drug use disorders commonly suffer from PTSD symptoms (Fuliilove et al., 1993). One study noted that as high as 90% of them reported a history of psychological trauma, and up to 50% fit the criteria for PTSD diagnosis (Chilcoat and Menard, 2003). Moreover, Nelson et al. (2002) found that people with a history of childhood sexual abuse or rape are prone to develop psychiatric disorders, such as depression, suicidality, as well as alcohol dependence, and nicotine dependence. Another study (Dannlowski et al., 2012) discovered that functional and structural neurological changes in the brains of people with a history of childhood abuse were similar to changes found in people suffering from depression and PTSD.

In conclusion, our earlier study followed a group of well-stabilized MMT patients with prolonged abstinence of at least 10 years and showed some difficulty in a specific situation of reverse learning (Levy-Gigi et al., 2014). Our current study did not find this pattern among a more heterogeneous cohort of patients receiving MMT. However, we did discover that patients in our clinic that have a history of childhood trauma showed a decreased ability to learn stimuli with a positive reward and an increased ability to learn stimuli with a negative outcome. These findings are consistent with some other studies that demonstrated a connection between traumatic life events, PTSD, and negative reward fixation.

Importantly, notice that in both studies the difficulty or impairment of performance was observed mainly in drug-related context. This fact reflect the daily life sensitivity to drug related cue, and the consistent need to work harder in any cognitive task to compensate the attention cue exist.

5. Study limitations

Our findings as based on results derived from small subgroups and their validation would require their application to a heterogeneous group of MMT patients with a history of childhood trauma and a psychiatric diagnosis of PTSD or complex PTSD. Our study design did not include the evaluation of PTSD or complex PTSD, and data on PTSD were available in the medical files of only a few patients.

Also, although task performance was not related to any variables including sex, age and history of self-harm or suicidal attempt that differed between the study groups, we cannot rule out that our study group tendency to negative rewards and stimuli stems from one or more of those characteristics. A bigger sample size involving more heterogeneous group of patients with a history of childhood trauma may clarify the amount of impact of those factors on negativity bias.

Conflict of interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2018.11.062.

References

Aas, M., Kauppi, K., Brandt, C.L., Tesli, M., Kaufmann, T., Steen, N.E., et al., 2017. Childhood trauma is associated with increased brain responses to emotionally negative as compared with positive faces in patients with psychotic disorders. Psychol. Med. 47, 669–679. https://doi.org/10.1017/S0033291716002762.

Anderson, N.H., 1965. Averaging versus adding as a stimulus-combination rule in impression formation. J. Exp. Psychol. 70, 394–400. https://doi.org/10.1037/h0022280.

Baumeister, R.F., Bratslavsky, E., Finkenauer, C., Vohs, K.D., 2001. Bad is stronger than good. Rev. Gen. Psychol. 5, 323–370.

Beck, A.T., 1987. Cognitive models of depression. J. Cogn. Psychother. 1 (1), 5–37. https://doi.org/9780826123077.

Bradley, B.P., Mogg, K., Lee, S.C., 1997. Attentional biases for negative information in induced and naturally occurring dysphoria. Behav. Res. Ther. 35, 911–927. https://doi.org/10.1016/S0005-7967(97)00053-3.

Burns, M.N., Lehman, K.A., Milby, J.B., Wallace, D., Schumacher, J.E., 2010. Do PTSD symptoms and course predict continued substance use for homeless individuals in contingency management for cocaine dependence? Behav. Res. Ther. 48, 588–598. https://doi.org/10.1016/j.brat.2010.03.010.

Camchong, J., MacDonald, A.W., Nelson, B., Bell, C., Mueller, B.A., Specker, S., et al., 2011. Frontal hyperconnectivity related to discounting and reversal learning in cocaine subjects. Biol. Psychiatry 69, 1117–1123. https://doi.org/10.1016/j.biopsych.2011.01.008.

Chilcoat, H.D., Menard, C., 2003. Epidemiological investigations: Comorbidity of posttraumatic stress disorder and substance use disorder. In: Ouimette, P., Brown, P.J. (Eds.), Trauma and Substance Abuse: Causes, Consequences, and Treatment of Comorbid Disorder. American Psychological Association, Washington, DC, pp. 9–28.

Constans, J.I., 2005. Information-processing biases in PTSD. In: Vasterling, J.J., Brewin, C. (Eds.), Neuropsychology of PTSD: Biological, Cognitive, and Clinical Perspectives. The Guilford Press, New York, pp. 105–130.

Dallery, J., Silverman, K., Chutuape, M.A., Bigelow, G.E., Stitzer, M.L., 2001. Voucher-based reinforcement of opiate plus cocaine abstinence in treatment-resistant methadone patients: Effects of reinforcer magnitude. Exp. Clin. Psychopharmacol. 9, 317–325. https://doi.org/10.1037/1064-1297.9.3.317.

Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., Grotegerd, D., et al., 2012. Limbic scars: Long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. Biol. Psychiatry 71, 286–293. https://doi.org/10.1016/j.biopsych.2011.10.021.

Elkana, O., Adelson, M., Doniger, G.M., Sason, A., Peles, E., 2017. Cognitive function is largely intact in methadone maintenance treatment patients. World J. Biol. Psychiatry 1–11. https://doi.org/10.1080/15622975.2017.1342047.

Elliott, R., Sahakian, B.J., McKay, A.P., Herrod, J.J., Robbins, T.W., Paykel, E.S., 1996. Neuropsychological impairments in unipolar depression: The influence of perceived failure on subsequent performance. Psychol. Med. 26, 975–989. https://doi.org/10.1017/S0033291700035303.

Engstrom, M., El-Bassel, N., Gilbert, L., 2012. Childhood sexual abuse characteristics, intimate partner violence exposure, and psychological distress among women in methadone treatment. J. Subst. Abuse Treat. 43, 366–376. https://doi.org/10.1016/j.jsat.2012.01.005.

Fani, N., Tone, E.B., Phifer, J., Norrholm, S.D., Bradley, B., Ressler, K.J., et al., 2012. Attention bias toward threat is associated with exaggerated fear expression and impaired extinction in PTSD. Psychol. Med. 42, 533–543. https://doi.org/10.1017/S0033291711001565.

Ford, J.D., Hawke, J., Alessi, S., Ledgerwood, D., Petry, N., 2007. Psychological trauma and PTSD symptoms as predictors of substance dependence treatment outcomes. Behav. Res. Ther. 45, 2417–2431. https://doi.org/10.1016/j.brat.2007.04.001.

Fuliilove, M.T., Fullilove, R.E., Michael, S., Winkler, K., Michael, C., Panzer, P.G., et al., 1993. Violence, trauma, and post-traumatic stress disorder among women drug users. J. Trauma. Stress 6, 533–543.

Hawks, R.L., 1987. Analytical methodology. NIDA Res. Monogr. 73, 30–42.

Herman, J.L., 1992. Complex PTSD: a syndrome in survivors of prolonged and repeated trauma. J. Trauma. Stress 5, 377–391. https://doi.org/10.1007/BF00977235.

Higgins, S.T., Silverman, K., 1999. Motivating Behavior Change Among Illicit-Drug

abusers: Research On Contingency Management Interventions. American Psychological Association, Washington, DC.
Johnson, S.W., North, R.A., 1992. Opioids excite dopamine neurons by hyperpolarization of local interneurons. J. Neurosci. 12, 483–488.
Kidorf, M., Stitzer, M.L., 1999. Contingent access to clinic privileges reduces drug abuse in methadone maintenance patients. Motivating Behavior Change Among Illicit-Drug Abusers: Research on Contingency Management Interventions. American Psychological Association, Washington, DC, pp. 221–241. https://doi.org/10.1037/10321-011.
Koob, G.F., Volkow, N.D., 2010. Neurocircuitry of addiction. Neuropsychopharmacology 35, 217–238. https://doi.org/10.1038/npp.2009.110.
Levy-Gigi, E., Kéri, S., Shapiro, A.R., Sason, A., Adelson, M., Peles, E., 2014. Methadone maintenance patients show a selective deficit to reverse positive outcomes in drug-related conditions compared to medication free prolonged opiate abstinence. Drug Alcohol Depend. 144, 111–118. https://doi.org/10.1016/j.drugalcdep.2014.08.016.
Lubman, D.I., Peters, L.A., Mogg, K., Bradley, B.P., Deakin, J.F.W., 2000. Attentional bias for drug cues in opiate dependence. Psychol. Med. 30, 169–175. https://doi.org/10.1017/S0033291799001269.
Mattick, R.P., Breen, C., Kimber, J., Davoli, M., 2014. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst. Rev. https://doi.org/10.1002/14651858.CD002207.pub4.
Máttyássy, A., Kéri, S., Myers, C.E., Levy-gigi, E., Gluck, M.A., Kelemen, O., 2012. Impaired generalization of associative learning in patients with alcohol dependence after intermediate-term abstinence. Alcohol Alcohol 47, 533–537. https://doi.org/10.1093/alcalc/ags050.
McLellan, A.T., Luborsky, L., O'Brien, C.P., Barr, H.L., Evans, F., 1984. The addiction severity index in three different populations. NIDA Res Monogr. 46, 217.
Meyer, W.J., Offenbach, S.I., 1961. Effectiveness of reward and punishment as a function of task complexity. J. Comp. Physiol. Psychol. 55, 532–534.
Nelson, E.C., Heath, A.C., Madden, P.A.F., Cooper, M.L., Dinwiddie, S.H., Bucholz, K.K., et al., 2002. Association between self-reported childhood sexual abuse and adverse psychosocial outcomes: Results from a twin study. Arch. Gen. Psychiatry 59, 139–145. https://doi.org/10.1001/archpsyc.59.2.139.
O'Brien, C.P., Childress, A.R., Ehrman, R., Robbins, S.J., 1998. Conditioning factors in drug abuse: Can they explain compulsion? J. Psychopharmacol. 12, 15–22. https://doi.org/10.1177/026988119801200103.
Quirk, G.J., Repa, J.C., LeDoux, J.E., 1995. Fear conditioning enhances short-latency auditory responses of lateral amygdala neurons: Parallel recordings in the freely behaving rat. Neuron 15, 1029–1039. https://doi.org/10.1016/0896-6273(95)90092-6.
Rass, O., Kleykamp, B.A., Vandrey, R.G., Bigelow, G.E., Leoutsakos, J.M., Stitzer, M.L., et al., 2014. Cognitive performance in methadone maintenance patients: Effects of time relative to dosing and maintenance dose level. Exp. Clin. Psychopharmacol 22, 248–256. https://doi.org/10.1037/a0035712.
Rowan, A.B., Foy, D.W., Rodriguez, N., Ryan, S., 1994. Posttraumatic stress disorder in a clinical sample of adults sexually abused as children. Child Abuse Neglect 18, 51–61.
Rozin, P., Royzman, E.B., 2001. Negativity bias, negativity dominance, and contagion. Personal. Soc. Psychol. Rev. 5, 296–320. https://doi.org/10.1207/S15327957PSPR0504_2.
Rustemeier, M., Römling, J., Czybulka, C., Reymann, G., Daum, I., Bellebaum, C., 2012. Learning from positive and negative monetary feedback in patients with alcohol dependence. Alcohol. Clin. Exp. Res. 36, 560–573. https://doi.org/10.1111/j.1530-0277.2011.01696.x.
Shook, N.J., Fazio, R.H., Vasey, M.W., 2007. Negativity bias in attitude learning: A possible indicator of vulnerability to emotional disorders? J. Behav. Ther. Exp. Psychiatry. 38, 144–155. https://doi.org/10.1016/j.jbtep.2006.10.005.
Silverman, K., Wong, C.J., Umbricht-Schneiter, A., Montoya, I.D., Schuster, C.R., Preston, K.L., 1998. Broad beneficial effects of cocaine abstinence reinforcement among methadone patients. J. Consult. Clin. Psychol. 66, 811–824. https://doi.org/10.1037/0022-006X.66.5.811.
Skowronski, J.J., Carlston, D.E., 1989. Negativity and extremity biases in impression formation: A review of explanations. Psychol. Bull. 105, 131–142. https://doi.org/10.1037/0033-2909.105.1.131.
Tiffany, S.T., 1990. A cognitive model of drug urges and drug-use behavior: Role of automatic and nonautomatic processes. Psychol. Rev. 97, 147–168. https://doi.org/10.1037/0033-295X.97.2.147.
Vogel, M., Dürsteler-MacFarland, K.M., Walter, M., Strasser, J., Fehr, S., Prieto, L., et al., 2011. Prolonged use of benzodiazepines is associated with childhood trauma in opioid-maintained patients. Drug Alcohol Depend. 119, 93–98. https://doi.org/10.1016/j.drugalcdep.2011.05.037.
Vythilingam, M., Blair, K.S., McCaffrey, D., Scaramozza, M., Jones, M., Nakic, M., et al., 2007. Biased emotional attention in post-traumatic stress disorder: A help as well as a hindrance? Psychol. Med. 37, 1445–1455. https://doi.org/10.1017/S003329170700092X.
Weinstock, J., Alessi, S.M., Petry, N.M., 2007. Regardless of psychiatric severity the addition of contingency management to standard treatment improves retention and drug use outcomes. Drug Alcohol Depend. 87, 288–296. https://doi.org/10.1016/j.drugalcdep.2006.08.027.
Wise, R.A., 2004. Dopamine, learning and motivation. Nat. Rev. Neurosci. 5, 483–494. https://doi.org/10.1038/nrn1406.