



Comparing the Facial Emotion Recognition in Opioid Antecedent Subjects and Mixed Opioid-methamphetamine Antecedent Subjects under Methadone Maintenance Therapy with Control Group-A Retrospective Cohort Study

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Received 2019 June 26; Revised 2021 March 04; Accepted 2021 March 13.

Abstract

Background: Facial emotion recognition (FER) is an important social skill. Some studies have determined the capability of FER in substance abusers, but their results are contradictory.

Objectives: This study aimed to investigate FER ability in opioid antecedent subjects and mixed opioid-methamphetamine antecedent subjects under methadone maintenance therapy compared to a control group.

Methods: Following a retrospective cohort design, 71 methadone-maintained subjects (MMS) (40 individuals with a history of only opioid use disorder and 31 patients with a history of both opioid and methamphetamine use disorder) and 40 healthy participants filled the Persian version of Ackman and Friesen facial emotion experiment, which were matched based on age, education, and gender. Demographic and substance use characteristics were evaluated. Both groups were similar concerning the duration of the opioid use disorder, methadone maintenance treatment, and currently prescribed methadone dose. Data were analyzed using the chi-square, independent t-test, one-way ANOVA, and Welch test. Statistical significance was considered when P-value < 0.05.

Results: Total FER scores were significantly lower in MMS compared to the control group. Concerning the subgroups, recognition of sadness was impaired in patients with a history of opioid use disorder (with and without a history of methamphetamine use disorder), while in recognition of anger and wonder, patients with both opioid and methamphetamine use disorder history had a significantly lower performance. There was no other significant difference between the groups.

Conclusions: The findings suggest that social cognition deficit should be considered in strategies related to the addiction (both treatment and rehabilitation).

Keywords: Emotions, Face, Identification, Methadone, Methamphetamine, Opioid

1. Background

Facial emotion expression (FEE) is defined as facial changes caused by internal emotional states, intentions, or social connections (1). In addition to the transfer of emotions, it can transmit intentions, physical efforts, and other interpersonal and intrapersonal feelings. The ability to recognize FEEs has a major role in non-verbal communication skills, which are necessary for successful compromise and environmental manipulation; hence, their absence may result in poor communication and disruptive

behavior (2). Previous studies showed that various disorders can intervene with the ability to recognize facial emotional representations. For instance, people with depressive disorders often suffer from significant problems in the identification of facial expressions (3). Also, those with obsessive-compulsive disorder, as opposed to depressed individuals, are less likely to recognize disgust and anger (4). In addition, studies conducted on patients with psychotic disorders such as schizophrenia reported impairments in recognition of FEE (5). Moreover, some studies on the FEE have especially focused on substance abusers; However,

conflicting results are reported. There is evidence regarding an association between the use of different types of substances and impaired facial emotion recognition (FER) (6-11). For instance, concerning alcohol abuse, some studies reported potential severe damages to the recognition of facial emotional manifestations. In addition, alcohol abusers have less accuracy in recognition of sadness and disgust, and they require more effort to recognize the emotional manifestations attributed to fear and anger (8, 12). Furthermore, Giuseppe Craparo et al. found that heroin addicts not only were slower in doing predefined tasks but also were less accurate in FER compared to healthy controls (11). Nejati et al. reported that cases with opium use disorder had lower performance in detection of sadness, happiness, and anger compared to the control group (13). On the other hand, Martin et al. demonstrated that patients with opiate use history who were on MMT had more accuracy in facial recognition of disgust compared to ex-opiate users. They also found that both opiate-exposed groups were similarly slower in recognition of sadness compared to the control group (14). Nonetheless, there are studies that found no difference in FER among substance users and healthy participants (15, 16). From a biological perspective, based on neuroscience studies, the insula, amygdala, anterior cingulate, and orbitofrontal cortex are important regions of the brain in the processing of facial expressions (17-20). There is also a line of evidence that suggests these regions are affected by substance abusers (19, 20). Hence, the deficit in FER ability is not unexpected. Nevertheless, some other studies did not succeed in reaching compelling results (15, 16, 21, 22).

Substance use disorders are relapsing and chronic global phenomena that can affect cognition, emotions, understanding, and social relations of affected people. It is worth noting that relapse is a major challenge that addiction therapists are usually faced. Impaired FER ability in substance users may cause misconceptions and disruption of social relations, which in turn may lead to interpersonal aggression and social alienation. These alterations may cause stress and negative feelings, which are associated with an increased risk of relapse and substance abuse continuation (9). Hence, better identification of different aspects of this problem is useful for the prevention of both the onset and recurrence of this harmful phenomenon (23).

2. Objectives

The current study aimed to investigate the FER ability in methadone-maintained subjects with and without a history of methamphetamine use disorder compared to the healthy control group.

3. Methods

3.1. Participants

Following a retrospective cohort design, volunteer participants were recruited from the private methadone clinics in the city of Ghaemshahr (north of Iran) from November to December 2018. Participants were categorized into three groups of methadone-maintained cases with a history of opioid use disorder (according to DSM-5 criteria) and methadone-maintained patients with a history of both opioid and methamphetamine use disorder (according to DSM-5 criteria) (two groups). Those in groups 1 and 2 were under methadone maintenance therapy (MMT) for at least 6 months and did not have a history of alcohol or other substance use disorder, except for nicotine. In addition, their multi-drug urine analysis on the experiment day was negative, except for the methadone. The exclusion criteria included being younger than 19 years old, race other than Mazani, history of any other psychiatric disorder, intellectual disability, history of head trauma with loss of consciousness for more than two minutes, any neurological disease, and visual impairment. All evaluations were performed by a psychiatrist, who was a member of the research team. Initially, three MMT clinics (as three clusters) were selected from three different regions of the city. For each group (patients with a history of only opioid use disorder and patients with both opioid and methamphetamine use disorders), a separate list of clients was prepared by emphasizing the variable of age. Then, a number of participants were selected randomly from each group. To match study groups concerning genetic and cultural characteristics, group 3 (controls) consisted only male healthy concomitants of those participants, who were matched concerning the variable of age. Because we could not find a sufficient number of female patients on MMT, in order to match study groups concerning the variable of gender, as a potentially confounding variable, we decided to only include male participants. For those in the control group, the multidrug urine analysis of all participants was negative on experiment day. The sample size was calculated using the G Power version 3.0.10. Also, the one-way ANOVA test was used for intragroup comparison of the FER score.

The sample size was estimated as 28 subjects per group (a total of 84 participants), based on the effect size (0.4) with a 95% confidence level ($\alpha = 5\%$, type I error), and a test power of 90% ($\beta = 10\%$, type II error). By considering a dropout rate of 50%, the number of participants in each group was increased to 42 subjects. Those with an incomplete questionnaire were excluded from the study. The study protocol of the current study is approved by the

Ethics Committee of the Mazandaran University of Medical Sciences (Reg. IR.MAZUMS.REC.1398324). In addition, after explaining the objectives and methodology of the study to all potential participants, written informed consent was obtained if agreeing. Initially, using some checklists, data on demographic characteristics and substance history of participants were collected. Afterward, participants were evaluated using the Ekman and Friesen facial expression experiment.

3.2. Instruments

3.2.1. Demographic and Substance History Checklist

Data on age, educational level, history of substance use disorder, and current MMT were collected using a self-report researcher-made questionnaire.

3.2.2. Ekman and Friesen Facial Expressions Experiment

Moosavian et al. Evaluated the validity of the Persian version of Ekman and Friesen facial expressions experiment on a sample of Iranians (24). The experiment contains 41 black and white photos of normal facial emotion expression. There were 6 photos for each of the fundamental emotions, including sadness, happiness, disgust, anger, wonder, and neutral state, while just 5 photos were related to the fear state. Initially, by showing a picture of each of the emotions, the type of emotion was taught to the individuals in order to ensure the sufficiency of their knowledge about the types of emotions. The pictures used at this stage were 7 cards (30 × 20 cm). Then, participants were asked to seat on a comfortable chair at a distance of 40 cm from the computer screen. After describing the experimental method, 41 other photos were displayed sequentially on a 16-inch tablet screen for 500 milliseconds. After submitting each photo, subjects had 5 seconds to name the emotion. The final results were calculated based on the total number of correct answers for each emotion. The overall score was equal to the sum of all emotions' scores. The experiment was carried out by an experienced psychologist who was blinded to study group allocation.

3.2.3. Statistical Analysis

Data were analyzed by SPSS version 21 using the chi-square test, independent *t*-test, one-way ANOVA, and Welch test (and Scheffe and Tamhane post hoc test). Statistical significance was considered when *P*-value < 0.05.

4. Results

A total of 71 male participants on MMT and 40 healthy male concomitants completed the study. The mean age of

participants was 37.02 ± 8.39 years. The youngest and oldest participants were 20 and 58 years old. There was no significant difference between the three groups concerning the variables of age and educational level. The mean duration of methamphetamine use was 4.83 ± 3.72 years, and for opioid use mean duration in groups 1 and 2 was 11.42 ± 7.56 and 11.26 ± 7.26 years, respectively. There was no significant difference between the two groups concerning the duration of opioid use. Also, the duration of MMT and current dose were similar between the two groups. The Levene's test was used to evaluate the equality of variances of age, duration of opioid use, duration of MMT, and current methadone dose variables between the study groups. Demographic characteristics and history of substance use of three study groups are described in Table 1.

One-way ANOVA revealed a statistically significant difference between the study groups. One-way ANOVA revealed an overall statistically significant difference in groups' means, regarding to total recognition, sadness, and anger and wonder score. According to Levene's test, the variance of variables of wonder and anger was not similar between the study groups. Therefore, a robust test (Welch) was used for these variables, and the results were in line with those of the ANOVA (Table 2).

Regarding the total recognition score, the post hoc test (Scheffe) demonstrated that the mean total FER score in groups 1 and 2 was significantly lower compared to the control group ($P = 0.005$ and $P = 0.001$, respectively). Also, those in groups 1 & 2 had lower performance in recognition of sadness compared to the control group ($P = 0.02$ and $P = 0.04$, respectively). Regarding recognition of wonder and anger, the Tamhane post hoc test showed that methadone-maintained patients with a history of both opioid and methamphetamine use disorder had a significantly lower ability to recognize wonder ($P = 0.011$) and anger ($P = 0.013$) compared to the control group.

5. Discussion

This study demonstrated a significant deficit in total FER accuracy score in methadone-maintained subjects (with and without a history of methamphetamine use disorder) compared to the healthy control group. Regarding the various type of emotions, recognition of sadness was impaired in patients with a history of opioid use disorder (with and without methamphetamine use disorder history), while in recognition of anger and wonder, patients with both opioid and methamphetamine use disorder history had significantly lower performance. Some studies evaluated the FER ability in individuals with a history of opiate use disorder; however, the reported results are contradictory. Kornreich et al. evaluated emotion recogni-

Table 1. Participants Demographic and Substance History Characteristics^a

Variable	Group 1 (n=40)	Group 2 (n=31)	Group 3 (n=40)	P-Value ^b
Age (mean ± SD)	38.45 ± 7.64	38.19 ± 7.41	34.70 ± 7.64	0.089
Education				0.124
Illiterate (n)	2	1	0	
Primary high school (n)	16	9	10	
Secondary high school (n)	12	18	18	
University (n)	10	3	12	
Duration of opioid use in year (mean ± SD)	11.42 ± 7.56	11.26 ± 7.26	-	0.925
Duration of methamphetamine use in year (mean ± SD)	-	4.83 ± 3.72	-	-
Duration of methadone maintenance treatment in year (mean ± SD)	5.45 ± 2.32	5.45 ± 2.25	-	0.998
Current methadone dose in milligram (mean ± SD)	69.75 ± 29.35	69.03 ± 31.02	-	0.921

^aGroup 1: methadone-maintained patients with a history of opioid use disorder; Group 2: methadone-maintained patients with a history of both opioid and methamphetamine use disorder; Group 3: healthy control subjects.

^bP-value < 0.05 was considered significant

tion performance in four groups of patients who underwent detoxification from alcohol recently, those with a history of opiate addiction on MMT, opiate addicts detoxified recently, detoxified patients with a history of both opiate and alcohol dependence. They reported that all participants had lower accuracy concerning the FER compared to the healthy controls (8). In the same vein, Giuseppe Craparo et al. showed that heroin-addicted participants not only were slower in doing the tasks but also had lower accuracy in FER compared to the healthy controls. They also reported that the deficit was correlated to the alexithymia score (11). Nejati et al. demonstrated that the performance of patients with opium use disorder in FER task was lower compared to the control group. Concerning the type of emotions, they reported that participants had less accuracy, only concerning the detection of sadness, happiness, and anger (13). The observed difference between the findings of the present study and some other studies can be attributed to the methodology of FER evaluation and the mean age of participants, which was higher in the present study (25). Meanwhile, Martin et al. demonstrated that patients with opiate use history who were on MMT obtained higher scores concerning the variable of recognition of facial display of disgust compared to the ex-opiate users (14). This result may be due to the increased exposure to others' facial expressions of disgust (14). In addition, there are various confounding variables such as culture and race. In contrast to the findings of the present study, they reported no difference concerning FER accuracy scores between the study groups. Probably, except for variables of race and cultural background, there are some other confounding factors that have contributed to this difference. For instance, we can mention exposure to

other substances like alcohol, crack, cannabis, and benzodiazepines 30 days prior to the test (14). Last but not least, Zhou et al. showed that abstinent heroin abusers had better performance in the detection of negative emotions (26). These results, as mentioned above, can be attributed to increased exposure to other facial expressions of negative emotions that may be influenced by culture and race. There are neurobiological evidence that can be used to explain the lower performance of addicts in emotional recognition tasks. Some previous studies reported impaired activity of various regions of the brain that are responsible for emotion processing including the insula, anterior cingulate, orbitofrontal cortex, and amygdala among drug users (13). Therefore, the deficit in FER ability is not unexpected. Moreover, in the present study, patients with no history of both opioid and methamphetamine use disorder had lower performance in total FER score, particularly regarding the detection of sadness, anger, and surprise. Consistent with the results of the present study, Henry et al. demonstrated that individuals with a history of methamphetamine dependence for at least six months of abstinence and currently engaged in rehabilitation programs had significant impairments in FER ability (10). In the same vein, Kim et al. reported that methamphetamine abusers had lower performance in FER and theory of mind tasks compared to the controls (9). Not surprising, they found a higher level of impaired recognition of fearful facial expressions in methamphetamine abusers compared to the control group. While, we found no significant difference between the study groups concerning the recognition of happiness, sadness, anger, and natural status. From a neurobiological perspective, the orbitofrontal cortex is the main part of the brain that has a role in the FER pro-

Table 2. Intra-Group Comparison of the Study Groups Concerning the Total Emotion Recognition Score and Different Types of Emotions^a

Group	Group 1 (n = 40)	Group 2 (n = 31)	Group 3 (n = 40)	Total (n = 111)	P Value ^b	F
Total recognition						
Mean ± SD	29.68 ± 4.38	28.81 ± 5.20	32.98 ± 3.91	30.57 ± 4.78	0.001	9.70
95%Confidence interval	28.27 - 31.08	26.74 - 30.49	31.73 - 34.22	29.67 - 31.47		
Happiness						
Mean ± SD	5.88 ± 0.40	5.81 ± 0.48	5.83 ± 0.68	5.84 ± 0.53	0.852	0.16
95%Confidence interval	5.75 - 6.00	5.63 - 5.19	5.61 - 6.04	5.74 - 5.94		
Sadness						
Mean ± SD	4.25 ± 1.37	4.26 ± 1.51	5.10 ± 1.19	4.56 ± 1.40	0.008	5.03
95%Confidence interval	3.81 - 4.69	3.71 - 4.81	4.72 - 5.48	4.30 - 4.82		
Fear						
Mean ± SD	1.60 ± 1.50	2.16 ± 1.21	2.33 ± 1.47	2.02 ± 1.44	0.063	2.84
95%Confidence interval	1.12 - 2.08	1.72 - 2.61	1.85 - 2.80	1.75 - 2.29		
Wonder						
Mean ± SD	5.40 ± 1.08	5.13 ± 1.15	5.78 ± 0.62	5.46 ± 0.99	0.011	4.83 ^c
95%Confidence interval	5.05 - 5.75	4.71 - 5.55	5.58 - 5.97	5.27 - 5.65		
Anger						
Mean ± SD	3.85 ± 1.70	3.13 ± 1.84	4.33 ± 1.37	3.82 ± 1.69	0.013	4.61 ^c
95%Confidence interval	3.82 - 1.69	2.45 - 3.80	3.89 - 4.76	3.50 - 4.14		
Disgust						
Mean ± SD	3.55 ± 1.99	3.55 ± 1.67	4.35 ± 1.63	3.84 ± 1.81	0.080	2.59
95%Confidence interval	2.91 - 4.19	2.94 - 4.16	3.83 - 4.87	3.50 - 4.18		
Natural						
Mean ± SD	5.15 ± 1.15	4.74 ± 1.16	5.28 ± 0.78	5.08 ± 1.05	0.089	2.47
95%Confidence interval	5.08 - 5.52	4.32 - 5.17	5.02 - 5.53	4.88 - 5.28		

^aGroup 1: methadone-maintained patients with a history of opioid use disorder; Group 2: methadone-maintained patients with a history of both opioid and methamphetamine use disorder; Group 3: healthy control subjects. Total recognition: total recognition score.

^bP-value < 0.05 considered significant.

^cWelch statistics

cess (27). There is a line of evidence that suggests that the orbitofrontal cortex undergoes some neurochemical and functional change in methamphetamine abusers. Those with a history of methamphetamine use had elevated and declined orbitofrontal glucose metabolism, respectively, in early and late abstinence (28, 29). Moreover, some studies reported declined orbitofrontal dopamine and serotonin transporters density in this population (30, 31). However, further studies are needed to extend our knowledge about these findings. Meanwhile, as mentioned above, some previous studies demonstrated a deficit in fear recognition in individuals with methamphetamine use disorder. Furthermore, there are evidence that some impairments in the amygdala activation in methamphetamine abusers compare to their healthy counterparts (9). The amygdala is an important part of the brain that has a ma-

major role in emotion recognition. Some neuropsychological studies showed that damage to the amygdala may lead to a deficit in recognizing negative facial emotion expressions, particularly fear, sadness, and disgust (32, 33). In the present study, groups 1 and 2 had significantly lower accuracy in the detection of facial expressions of sadness, but there was no difference between the three groups concerning the ability to recognize fear and disgust. It can be attributed to factors such as a history of concomitant use of opioids that should be considered as a potential confounding factor.

Moreover, in the present study, patients with a history of opioid use disorder (with and without methamphetamine use disorder history) were on MMT. Hence, methadone use should be considered as a confounding factor. Previous studies demonstrated that methadone

may cause acute-on-chronic sedative effects when is administered in opiate users (34, 35). Besides, methadone can decrease the speed of psychomotor activity (36, 37). Hence, it can be assumed that impaired cognitive ability due to methadone consumption probably has affected the results. In our patients, methadone dose and duration of methadone therapy were similar between the study groups. Therefore, if we accept that methadone treatment leads to impaired detection of sadness and overall deficit in facial emotion expression, lower performance of patients with a history of both opioid and methamphetamine use disorder in recognizing wonder and anger cannot be justified. Also, as mentioned before, some differences between the results of this research and previous studies may be due to the applied methodology such as used tasks, heterogeneity in gender, age, and other concomitant substances use, particularly alcohol.

Generally, it seems that the findings of the present study are in line with most of the previous studies and provide further support to assert deficit in FER performance in patients with a history of substance use disorder. Nowadays, it is well proved that the ability to identify facial emotional expression is an important social skill; hence, impairment in this area may result in social communication problems, which may lead to distress and negative feelings that in turn may result in an increased risk of relapse. Hence, it is necessary to consider this impairment in treatment and rehabilitation strategies in order to achieve better outcomes.

It is necessary to mention some limitations and strengths of our study. The most important strength of this study was matching the study groups concerning the confounding factors like gender, age, race, education level, and history of other substance abuse; however, personal traits were not considered in the study. Hence, it can be considered as a potential source of bias. Moreover, we did not evaluate other cognitive domains. Moreover, caution should be taken when generalizing the findings, as the findings are related to a particular sample in a single city. Future studies should consider other confounders related to functional neuroimaging and cellular and molecular evaluations, which will improve the clarity of different aspects of social cognition.

5.1. Conclusions

This study demonstrated that patients with opioid use disorder and those with both opioid and methamphetamine use disorder had a lower level of FER compared to the controls. Given that deficit in FER may cause various difficulties in interpersonal relations, social cognition deficit should be considered in strategies related to the addiction (both treatment and rehabilitation).

Footnotes

Authors' Contribution: Kamaledin Alaedini was responsible for the design of the study, interpretation of findings, and writing the draft paper. Maryam Farahmandfar contributed to study design and review the manuscript draft. Maryam Sefidgarnia contributed to study the design and edition of the manuscript draft. Parisa Eslami assisted with data analysis. Sepideh Jafari contributed to the acquisition of data. All authors critically reviewed content and approved the final version for publication.

Conflict of Interests: None.

Ethical Approval: All aspects of the study protocol were approved by the ethics committee of Mazandaran University of Medical Sciences (Reg.IR.MAZUMS.REC.1398324).

Funding/Support: None.

Informed Consent: All participants signed the informed consent form.

References

- Ekman P. Oxford EJV&S. *The argument and evidence about universals in facial expressions. Handbook of social psychophysiology.* 1989. p. 143-64.
- Amenta SFC, Balconi M. Facial expression decoding in autistic and asperger children. *Comprehensive Guide to Autism.* New York: Springer; 2014.
- Abdollah Ghasempour, Samad Fahimi, Abbas Abolghasemi, Ahmad Amiri, Ali Fakhari; Ebrahim Akbari, et al. [Recognition of facial expression of emotion in patients with depression and normal people]. *YJMS.* 2012;**14**(1):91-8. Persian.
- Ghasempour A, Fahimi S, Amiri A, Akbari E, Abolghasemi A, Fakhari A. Comparing the recognition of emotional facial expressions in patients with obsessive-compulsive and major depression. *ZJRMS.* 2014;**16**(5):59-62.
- Lahera G, Herrera S, Fernandez C, Bardón M, de los Angeles V, Fernandez-Liria A. Familiarity and face emotion recognition in patients with schizophrenia. *Compr Psychiatry.* 2014;**55**(1):199-205. doi: [10.1016/j.comppsy.2013.06.006](https://doi.org/10.1016/j.comppsy.2013.06.006). [PubMed: [23993221](https://pubmed.ncbi.nlm.nih.gov/23993221/)].
- Yip JT, Lee TM. Selective impairment of sadness and disgust recognition in abstinent ecstasy users. *Neuropsychologia.* 2006;**44**(6):959-65. doi: [10.1016/j.neuropsychologia.2005.10.001](https://doi.org/10.1016/j.neuropsychologia.2005.10.001). [PubMed: [16293272](https://pubmed.ncbi.nlm.nih.gov/16293272/)].
- Bayrakci A, Sert E, Zorlu N, Erol A, Saricicek A, Mete L. Facial emotion recognition deficits in abstinent cannabis dependent patients. *Compr Psychiatry.* 2015;**58**:160-4. doi: [10.1016/j.comppsy.2014.11.008](https://doi.org/10.1016/j.comppsy.2014.11.008). [PubMed: [25550274](https://pubmed.ncbi.nlm.nih.gov/25550274/)].
- Kornreich C, Foisy ML, Philippot P, Dan B, Tecco J, Noel X, et al. Impaired emotional facial expression recognition in alcoholics, opiate dependence subjects, methadone maintained subjects and mixed alcohol-opiate antecedents subjects compared with normal controls. *Psychiatry Res.* 2003;**119**(3):251-60. doi: [10.1016/S0165-1781\(03\)00130-6](https://doi.org/10.1016/S0165-1781(03)00130-6). [PubMed: [12914896](https://pubmed.ncbi.nlm.nih.gov/12914896/)].
- Kim YT, Kwon DH, Chang Y. Impairments of facial emotion recognition and theory of mind in methamphetamine abusers. *Psychiatry Res.* 2011;**186**(1):80-4. doi: [10.1016/j.psychres.2010.06.027](https://doi.org/10.1016/j.psychres.2010.06.027). [PubMed: [20643485](https://pubmed.ncbi.nlm.nih.gov/20643485/)].
- Henry JD, Mazur M, Rendell PG. Social-cognitive difficulties in former users of methamphetamine. *Br J Clin Psychol.* 2009;**48**(Pt 3):323-7. doi: [10.1348/000712609X435742](https://doi.org/10.1348/000712609X435742). [PubMed: [19397848](https://pubmed.ncbi.nlm.nih.gov/19397848/)].

11. Craparo G, Gori A, Dell'Aera S, Costanzo G, Fasciano S, Tomasello A, et al. Impaired emotion recognition is linked to alexithymia in heroin addicts. *PeerJ*. 2016;**4**. e1864. doi: [10.7717/peerj.1864](https://doi.org/10.7717/peerj.1864). [PubMed: [27069803](https://pubmed.ncbi.nlm.nih.gov/27069803/)]. [PubMed Central: [PMC4824882](https://pubmed.ncbi.nlm.nih.gov/PMC4824882/)].
12. Felisberti F, Terry P. The effects of alcohol on the recognition of facial expressions and microexpressions of emotion: enhanced recognition of disgust and contempt. *Hum Psychopharmacol*. 2015;**30**(5):384-92. doi: [10.1002/hup.2488](https://doi.org/10.1002/hup.2488). [PubMed: [26073552](https://pubmed.ncbi.nlm.nih.gov/26073552/)].
13. Nejati V, Shiri E, Nuri Z. Comparison of emotion recognition and mind reading abilities in opium abusers and healthy matched individuals. *Research on Addiction*. 2012;**6**(21):19-30.
14. Martin L, Clair J, Davis P, O'Ryan D, Hoshi R, Curran HV. Enhanced recognition of facial expressions of disgust in opiate users receiving maintenance treatment. *Addiction*. 2006;**101**(11):1598-605. doi: [10.1111/j.1360-0443.2006.01574.x](https://doi.org/10.1111/j.1360-0443.2006.01574.x). [PubMed: [17034439](https://pubmed.ncbi.nlm.nih.gov/17034439/)].
15. Woicik PA, Moeller SJ, Alia-Klein N, Maloney T, Lukasik TM, Yeliosof O, et al. The neuropsychology of cocaine addiction: recent cocaine use masks impairment. *Neuropsychopharmacology*. 2009;**34**(5):1112-22. doi: [10.1038/npp.2008.60](https://doi.org/10.1038/npp.2008.60). [PubMed: [18496524](https://pubmed.ncbi.nlm.nih.gov/18496524/)]. [PubMed Central: [PMC2667096](https://pubmed.ncbi.nlm.nih.gov/PMC2667096/)].
16. Hulka LM, Preller KH, Vonmoos M, Broicher SD, Quednow BB. Cocaine users manifest impaired prosodic and cross-modal emotion processing. *Front Psychiatry*. 2013;**4**:98. doi: [10.3389/fpsy.2013.00098](https://doi.org/10.3389/fpsy.2013.00098). [PubMed: [24046750](https://pubmed.ncbi.nlm.nih.gov/24046750/)]. [PubMed Central: [PMC3763688](https://pubmed.ncbi.nlm.nih.gov/PMC3763688/)].
17. Sato W, Kochiyama T, Yoshikawa S. The inversion effect for neutral and emotional facial expressions on amygdala activity. *Brain Res*. 2011;**1378**:84-90. doi: [10.1016/j.brainres.2010.12.082](https://doi.org/10.1016/j.brainres.2010.12.082). [PubMed: [21215733](https://pubmed.ncbi.nlm.nih.gov/21215733/)].
18. Davidson RJ, Slagter HA. Probing emotion in the developing brain: functional neuroimaging in the assessment of the neural substrates of emotion in normal and disordered children and adolescents. *Ment Retard Dev Disabil Res Rev*. 2000;**6**(3):166-70. doi: [10.1002/1098-2779\(2000\)6:3<166::AID-MRDD3>3.0.CO;2-O](https://doi.org/10.1002/1098-2779(2000)6:3<166::AID-MRDD3>3.0.CO;2-O). [PubMed: [10982493](https://pubmed.ncbi.nlm.nih.gov/10982493/)].
19. Naqvi NH, Bechara A. The hidden island of addiction: The insula. *Trends Neurosci*. 2009;**32**(1):56-67. doi: [10.1016/j.tins.2008.09.009](https://doi.org/10.1016/j.tins.2008.09.009). [PubMed: [18986715](https://pubmed.ncbi.nlm.nih.gov/18986715/)]. [PubMed Central: [PMC3698860](https://pubmed.ncbi.nlm.nih.gov/PMC3698860/)].
20. Di Chiara G, Tanda G, Bassareo V, Pontieri F, Acquas E, Fenu S, et al. Drug addiction as a disorder of associative learning. Role of nucleus accumbens shell/extended amygdala dopamine. *Ann N Y Acad Sci*. 1999;**877**:461-85. doi: [10.1111/j.1749-6632.1999.tb09283.x](https://doi.org/10.1111/j.1749-6632.1999.tb09283.x). [PubMed: [10415665](https://pubmed.ncbi.nlm.nih.gov/10415665/)].
21. Verdejo-Garcia A, Perez-Garcia M, Bechara A. Emotion, decision-making and substance dependence: a somatic-marker model of addiction. *Curr Neuropharmacol*. 2006;**4**(1):17-31. doi: [10.2174/157015906775203057](https://doi.org/10.2174/157015906775203057). [PubMed: [18615136](https://pubmed.ncbi.nlm.nih.gov/18615136/)]. [PubMed Central: [PMC2430678](https://pubmed.ncbi.nlm.nih.gov/PMC2430678/)].
22. Donadon MF, Osorio Fde L. Recognition of facial expressions by alcoholic patients: a systematic literature review. *Neuropsychiatr Dis Treat*. 2014;**10**:1655-63. doi: [10.2147/NDT.S65376](https://doi.org/10.2147/NDT.S65376). [PubMed: [25228806](https://pubmed.ncbi.nlm.nih.gov/25228806/)]. [PubMed Central: [PMC4161523](https://pubmed.ncbi.nlm.nih.gov/PMC4161523/)].
23. Peyravi H, Alavi SS, Ghanizadeh M. The effect of compliance with group therapy on quality of life, global function and care after treatment in opium addicted under mmt (methadone maintenance therapy). *Iran Journal of Nursing*. 2018;**30**(110):45-57. doi: [10.29252/ijn.30.110.45](https://doi.org/10.29252/ijn.30.110.45).
24. Moosavian E, Mohammadi N. [A comparison of the recognition of disgust between patients with severe obsessive-compulsive disorder and healthy people]. *J R Psychol Health*. 2016;**9**(14):11-9. Persian.
25. Castellano F, Bartoli F, Crocamo C, Gamba G, Tremolada M, Santambrogio J, et al. Facial emotion recognition in alcohol and substance use disorders: A meta-analysis. *Neurosci Biobehav Rev*. 2015;**59**:147-54. doi: [10.1016/j.neubiorev.2015.11.001](https://doi.org/10.1016/j.neubiorev.2015.11.001). [PubMed: [26546735](https://pubmed.ncbi.nlm.nih.gov/26546735/)].
26. Zhou Y, Zhu H, Jin X, Li X, Zhang M, Zhang F, et al. Biased attention towards negative schematic expression in abstinent heroin abusers. *J Behav Ther Exp Psychiatry*. 2012;**43**(2):705-10. doi: [10.1016/j.jbtep.2011.10.004](https://doi.org/10.1016/j.jbtep.2011.10.004). [PubMed: [22080167](https://pubmed.ncbi.nlm.nih.gov/22080167/)].
27. Rolls ET. The representation of information about faces in the temporal and frontal lobes. *Neuropsychologia*. 2007;**45**(1):124-43. doi: [10.1016/j.neuropsychologia.2006.04.019](https://doi.org/10.1016/j.neuropsychologia.2006.04.019). [PubMed: [16797609](https://pubmed.ncbi.nlm.nih.gov/16797609/)].
28. London ED, Simon SL, Berman SM, Mandelkern MA, Lichtman AM, Bramen J, et al. Mood disturbances and regional cerebral metabolic abnormalities in recently abstinent methamphetamine abusers. *Arch Gen Psychiatry*. 2004;**61**(1):73-84. doi: [10.1001/archpsyc.61.1.73](https://doi.org/10.1001/archpsyc.61.1.73). [PubMed: [14706946](https://pubmed.ncbi.nlm.nih.gov/14706946/)].
29. Volkow ND, Chang L, Wang GJ, Fowler JS, Ding YS, Sedler M, et al. Low level of brain dopamine D2 receptors in methamphetamine abusers: association with metabolism in the orbitofrontal cortex. *Am J Psychiatry*. 2001;**158**(12):2015-21. doi: [10.1176/appi.ajp.158.12.2015](https://doi.org/10.1176/appi.ajp.158.12.2015). [PubMed: [11729018](https://pubmed.ncbi.nlm.nih.gov/11729018/)].
30. Sekine Y, Minabe Y, Ouchi Y, Takei N, Iyo M, Nakamura K, et al. Association of dopamine transporter loss in the orbitofrontal and dorsolateral prefrontal cortices with methamphetamine-related psychiatric symptoms. *Am J Psychiatry*. 2003;**160**(9):1699-701. doi: [10.1176/appi.ajp.160.9.1699](https://doi.org/10.1176/appi.ajp.160.9.1699). [PubMed: [12944350](https://pubmed.ncbi.nlm.nih.gov/12944350/)].
31. Sekine Y, Ouchi Y, Takei N, Yoshikawa E, Nakamura K, Futatsubashi M, et al. Brain serotonin transporter density and aggression in abstinent methamphetamine abusers. *Arch Gen Psychiatry*. 2006;**63**(1):90-100. doi: [10.1001/archpsyc.63.1.90](https://doi.org/10.1001/archpsyc.63.1.90). [PubMed: [16389202](https://pubmed.ncbi.nlm.nih.gov/16389202/)].
32. Adolphs R, Tranel D, Hamann S, Young AW, Calder AJ, Phelps EA, et al. Recognition of facial emotion in nine individuals with bilateral amygdala damage. *Neuropsychologia*. 1999;**37**(10):1111-7. doi: [10.1016/S0028-3932\(99\)00039-1](https://doi.org/10.1016/S0028-3932(99)00039-1). [PubMed: [10509833](https://pubmed.ncbi.nlm.nih.gov/10509833/)].
33. Schmolck H, Squire LR. Impaired perception of facial emotions following bilateral damage to the anterior temporal lobe. *Neuropsychology*. 2001;**15**(1):30-8. [PubMed: [11216887](https://pubmed.ncbi.nlm.nih.gov/11216887/)].
34. Curran HV, Bolton J, Wanigaratne S, Smyth C. Additional methadone increases craving for heroin: a double-blind, placebo-controlled study of chronic opiate users receiving methadone substitution treatment. *Addiction*. 1999;**94**(5):665-74. doi: [10.1046/j.1360-0443.1999.9456654.x](https://doi.org/10.1046/j.1360-0443.1999.9456654.x). [PubMed: [10563031](https://pubmed.ncbi.nlm.nih.gov/10563031/)].
35. Curran HV, Kleckham J, Bearn J, Strang J, Wanigaratne S. Effects of methadone on cognition, mood and craving in detoxifying opiate addicts: a dose-response study. *Psychopharmacology (Berl)*. 2001;**154**(2):153-60. doi: [10.1007/s002130000628](https://doi.org/10.1007/s002130000628). [PubMed: [11314677](https://pubmed.ncbi.nlm.nih.gov/11314677/)].
36. Hiltunen AJ, Lafolie P, Martel J, Ottosson EC, Boreus LO, Beck O, et al. Subjective and objective symptoms in relation to plasma methadone concentration in methadone patients. *Psychopharmacology (Berl)*. 1995;**118**(2):122-6. doi: [10.1007/BF02245829](https://doi.org/10.1007/BF02245829). [PubMed: [7617797](https://pubmed.ncbi.nlm.nih.gov/7617797/)].
37. Mintzer MZ, Stitzer ML. Cognitive impairment in methadone maintenance patients. *Drug Alcohol Depend*. 2002;**67**(1):41-51. doi: [10.1016/S0376-8716\(02\)00013-3](https://doi.org/10.1016/S0376-8716(02)00013-3). [PubMed: [12062778](https://pubmed.ncbi.nlm.nih.gov/12062778/)].