Life Sciences 233 (2019) 116712

Contents lists available at ScienceDirect

Life Sciences

journal homepage: www.elsevier.com/locate/lifescie

Possible involvement of nucleus accumbens D1-like dopamine receptors in the morphine-induced condition place preference in the offspring of morphine abstinent rats

Mitra-Sadat Sadat-Shirazi[a], Nazanin Monfared Neirizi[a], Maral Matloob[a], Mohammad Safarzadeh[a], Mojtaba Behrouzi[a], Aryaan Rajabpoor Dehdashti[a], Ghorbangol Ashabi[b], Mohammad-Reza Zarrindast[a,c,d,*]

[a] Iranian National Center for Addiction Studies (INCAS), Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[c] Pharmacology Department, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[d] Endocrinology and Metabolism Research Institute, Tehran University of Medical Science, Tehran, Iran

ARTICLE INFO

Keywords:
Morphine
Offspring
Nucleus accumbens
D1 dopamine receptor
CPP

ABSTRACT

Aims: Previous researches demonstrated that genetics and environment are two essential factors to prone individuals to drug abuse. Our previous data showed that dopaminergic system changed in the offspring of morphine-abstinent rats. In the present study, we evaluated whether blocking the D1-like dopamine receptors (DR) in the nucleus accumbens (NAC) affect the rewarding effect of morphine in the offspring of morphine-abstinent rats.

Main methods: In the study, male and female Wistar rats received morphine orally for 21 days. Ten days after last morphine administration, animals prepared to mate either with a morphine abstinent or a drug-naive rat. Adult male offspring were chosen for further evaluation. SCH23390 (0.01 μg/rat) was administrated intra-NAC during the conditioning phase in the CPP paradigm (morphine 7.5 mg/kg).

Key findings: Obtained data showed that morphine administration (7.5 mg/kg) did not induce conditioning in the offspring of the morphine-abstinent parent(s) ($p < 0.001$) compared with the control group. However, when SCH23390 injected in the NAC during the induction phase, the offspring of morphine-abstinent rats were conditioned with the same dose of morphine.

Significance: Previous studies showed that the offspring of morphine-abstinent rats are more prone to opioid consumption, and also developed tolerance to the rewarding effect of morphine. Current data indicated that blockade of D1-like DR in the NAC could prevent morphine-induced tolerance in these offspring. Therefore, inhibition of D1-like DR in the NAC might be a new candidate against morphine-reinforcing effect in the offspring of morphine-abstinent parent(s).

1. Introduction

Opiate – a product of opium poppy – is a commonly misused drug in the Middle East. Opioids are the most common pain killer used for managing moderate to severe pain [1]. Although, after using prescribed opioids, someone might be addicted [2]. Both genetic predispositions and environmental conditions involved in the risk of developing opioid addiction [3–5]. Besides, exposure to opioids during development (in the uterus) induced psychological disorders in the offspring [6,7].

Reward is described as any incident that increases response with a positive hedonic element. The mesocortical dopamine system is a fundamental component of the reward system. This system also has an essential role in drug abuse disorder [8]. Positron emission tomography studies indicated that alcohol and other drugs of abuse increase dopamine and opioid peptides in the ventral striatum [9,10]. It is well established that all kinds of drugs of abuse stimulate the Ventral Tegmental Area (VTA) dopaminergic neurons. These neurons projected to NAC and released dopamine there, which leads to reward response [11–14]. Enhancing in dopamine is associated with “high” sensation in abusers, which is related to the activation of the dopamine receptor

* Corresponding author at: Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, P.O. Box 13145-784, Tehran, Iran.
E-mail address: zarinmr@ams.ac.ir (M.-R. Zarrindast).

https://doi.org/10.1016/j.lfs.2019.116712
Received 4 June 2019; Received in revised form 22 July 2019; Accepted 30 July 2019
Available online 01 August 2019
0024-3205/

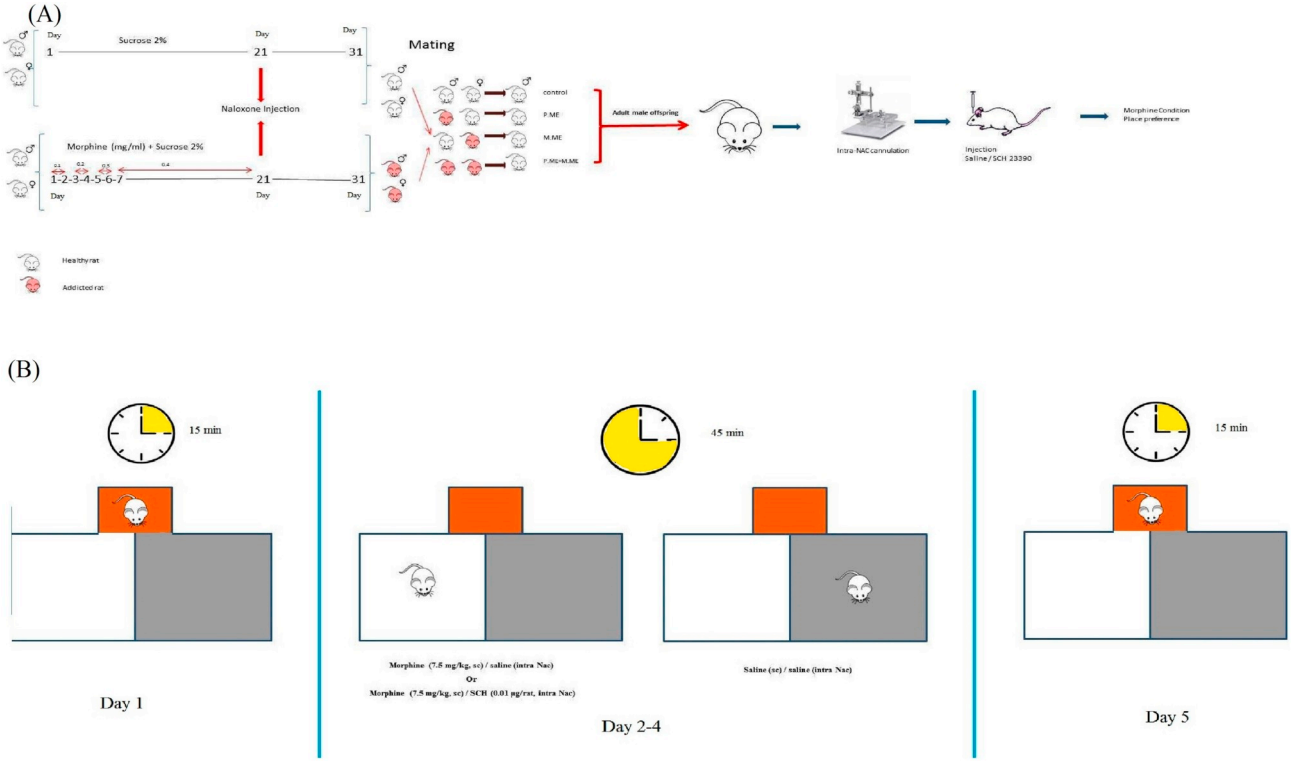

Fig. 1. A schematic diagram of the study design (A) and behavioral test (B). M.ME, maternal morphine-exposed offspring; P.ME, paternal morphine-exposed offspring.

(DR) type 1 [8]. It has been shown that dopaminergic system has a significant role in drug abuse; changing in the dopaminergic system causes the descendants of addicted parents to have tolerance in reinforcing [15] and antinociceptive [16] properties of opioids.

Dopamine receptor (DR) type 1, which coupled with stimulatory G protein (Gs), widely expressed in the mesocortical and mesolimbic regions [17]. D1-like DR family contains two receptors: D1-DR and D5-DR. Both D1 and D5 DR share common pharmacological features [17]. In the intoxication phase, the enormous amount of dopamine released and D1-like DRs are activated in this phase [18]. Also, conditioning induced by drugs needs the stimulation of D1-like DR [19]. D1-like DRs are located on dopaminergic neurons. In the axon terminal site, D1-like DR activation leads to enhance excitability via increasing NMDA glutamate receptor, T-Type calcium channel, and the current of sodium channels [20].

cAMP response element binding protein (CREB) is a transcription factor and play as a critical mediator of adaptations induced by drugs of abuse [21]. After chronic morphine exposure, the amount of p-CREB increased in the brain, which modulation of CREB has a prominent role in plasticity induced by opioids [22]. It has been shown that Mitogen-Activated Protein Kinase (MAPK) cascade, that CREB is one of its downstream, has a major role in developing morphine tolerance [23].

It has been demonstrated that parental morphine exposure even before gestation induced devastating behavioral and molecular changes in the offspring [15,16,24–26]. The conditioned place preference (CPP) paradigm that is based on Pavlovian conditioning is a widely used animal model for investigating the reinforcing effect of drugs of abuse [27]. It has been stated that the choice of animals in the CPP paradigm might be underlying the rewarding properties and abuse potential of drugs [28]. Previously, we showed that the offspring of morphine-abstinent parents exhibit tolerance to the reinforcing effect of morphine in the CPP paradigm [15,24].

According to the vital role of dopamine in the induction of CPP [29] and tolerance [30], the current study was designed to investigate the role of D1-like DR located in the NAC on morphine-tolerance induced in the offspring of morphine-abstinent parents.

2. Material and method

2.1. Animals and drugs

Male and female adult Wistar rats (with the age of 60 days and the weight range of 250–300 g) were purchased from the Pasteur Institute (Tehran, Iran). Four rats were kept in a standard cage in a temperature-controlled environment (22 ± 2 °C) and a 12/12 h light/dark cycle (light beginning at 7 A.M.) with ad libitum access to food and water. All experiments were conducted during the light phase of the light/dark cycle. It should be noted that all animals were used once only.

Drugs used in this study were morphine sulfate (Faran Shimi Co. Tehran, Iran), sucrose (Merck, Germany), SCH23390 (Tocris, UK), ketamine hydrochloride (50 mg/kg) and xylazine (4 mg/kg). Morphine sulfate was dissolved in distilled water for oral use. Sucrose (Merck, Germany) was used to lower the bitterness of morphine. Ketamine hydrochloride and xylazine were used for anesthesia at the beginning of the stereotaxic procedure.

2.2. Parental morphine exposure

Female and male rats received morphine orally by dissolving it in their drinking water for 21 days, as was described previously [25]. Morphine solution doses of 0.1, 0.2 and 0.3 mg/ml were administered for the first six days; each dose was applied for two days, respectively, then the 0.4 mg/ml dose was used for the remaining 15 days. The bitter taste of morphine was eliminated by adding 2% sucrose to the morphine solution. Control group only received sucrose in their drinking water.

2.3. Mating protocol

After the 21 days of drug administration, the animals remained drug-free for ten days. Animals were prepared for mating after the ten days of prohibition. One female and one male rat were placed in each

cage for mating, according to Fig. 1. The animals were classified into four categories. The categories are as follows:

Category 1: drug-naïve male and female; male offspring named as control

Category 2: morphine-abstinent male and drug-naïve female; male offspring named as Paternal Morphine-Exposed (P.ME)

Category 3: drug-naïve male and morphine-abstinent female; male offspring named as Maternal Morphine-Exposed (M.ME)

Category 4: morphine-abstinent male and female; male offspring named as Paternal and Maternal Morphine-Exposed (P + M.ME)

2.4. Stereotaxic surgery and microinjections

Offspring were undergone stereotaxic surgery. All animals were anesthetized using ketamine hydrochloride (50 mg/kg) and xylazine (4 mg/kg) via intraperitoneal injection. Then the animals were weighed and injected with the solution based on their weight. After the application of anesthesia, all the rats were placed and fixed in a stereotaxic apparatus. Two stainless steel cannulae (22 gauge) were implanted in the Nucleus Accumbens shell in both sides of the brain. Regions and coordinates were duplicated from the Atlas of Paxinos and Watson [31]. Coordinates for the NAC regions were as follows: +0.96 mm anterior to bregma, ± 0.8 mm lateral to Midline and −7 mm ventral to the dorsal surface of the skull. The two cannulae were fixed on the skull using acrylic dental paste. The rats were allowed to recover from the surgery for seven days before the CPP test. In order to perform the injections, thinner inner cannula (gauge 27), in order to slide through the main cannulae (fixed on the skull). The inner cannula is connected to a Hamilton syringe by polyethylene tube. A volume of 0.5 μl of SCH23390 solution was injected in each NAC in 60 s. The cannulae were kept inside for an additional 60 s to allow diffusion of the solution and to reduce the possibility of reflux.

2.5. Conditioned place preference (CPP)

2.5.1. Apparatus

The CPP apparatus used in this study consisted of three wooden chambers. Two of them (chambers A and B) were of equal sizes (40 × 30 × 30 cm) with a different shape. Chamber A had a textured floor with black horizontal stripes on its white walls. Chamber B had a smooth floor with vertical white stripes on its black walls. The width of the stripes was 2 cm in both chambers. The third chamber's (chamber C) dimensions were different from the other two, and it was orange colored. The C chamber was attached to the rear side of the other two chambers, and they were separated using two guillotine doors which were manually operated. Therefore when the sliding doors were opened, animals could roam in these three chambers freely.

2.5.2. Behavioral test

The CPP test is used to determine the rewarding and reinforcing effects of drugs such as morphine [32]. Rats instinctively prefer to settle in the darker chamber (B), but if they are to be drugged to remain in a less preferred place (A) after conditioning, they will settle in the drug-paired chamber even though they are not going to receive any drugs. The test was carried out on five consecutive days and had three following stages:

A) Pre-conditioning

In the first day, the animal was placed in the C chamber with sliding doors lifted; so that it could move freely between the rooms and get familiarized with all the chambers for 15 min. The animal's movement was recorded using a camera installed approximately 50 cm above the CPP apparatus. The total time (s) spent in each chamber was measured.

B) Conditioning

The conditioning stage was set out on day 2 until day 4. There were two 45-minute sessions per day with a 6-hour interval (first session beginning at 7 A.M. and the second session at 1 P.M.). Before starting the experiment, rats were left in the CPP test room for approximately 10 min. During the conditioning phase (days 2 and 4), rats were injected with morphine solution (7.5 mg/kg) subcutaneously, then SCH23390 was injected into the NAC. Immediately after injections, they were confined in Chamber A (less preferred, also known as drug-paired) for 45 min. The second session took place at 1 P.M. on the same day, and animals only received saline (both s.c. and Intra-NAC). In day 3, the entire procedure of the aforementioned experiment was completely reversed, meaning that the rats in all categories alternately received placebo and the drugs.

C) Post-conditioning

The post-conditioning stage or the testing stage was performed on the fifth day (1 day after the last conditioning day). Each animal was placed in the C chamber with all the sliding doors lifted so that it could roam all the chambers freely for 15 min. The total time (s) spent in each chamber was measured and reported. According to the other studies [33–36], the preference score was calculated as follows:

Preference score
= the total time in the drug − paired chamber on the post
− conditioning day − the total time spent on the drug
− paired chamber on the pre − conditioning day

2.6. Experimental design

2.6.1. The effect of intra-NAC administration of SCH23390 on morphine induced condition place preference in drug-naïve offspring

This experiment was designed to assess the effect of intra-NAC administration of SCH23390 (as a D1DR antagonist) on morphine-induced conditioning in the drug-naïve offspring. According to our previous study [15], we chose the dose of morphine (7.5 mg/kg) that induced conditioning in the drug-naïve offspring but did not elicit reinforcing effect on the offspring of morphine-abstinent parents. In this experiment, three groups of animals (a total of 24 rats, N = 8 per group) were used to figure out the dose-response curve for SCH23390. The dose of SCH23390 that block morphine-induced conditioning was chosen.

2.6.2. The effect of intra-NAC administration of SCH23390 on morphine-induced conditioning in the offspring of morphine-abstinent parents

This experiment was designed to determine whether inhibition of D1DR located in the NAC affect morphine CPP in the offspring of morphine-abstinent rats. In this experiment, two groups from each category (N = 8 per group) were used. The first set received morphine (7.5 mg/kg, s.c.) and saline (intra-NAC) during conditioning. The second set of animals received morphine (7.5 mg/kg, s.c.) and SCH23390 (0.01 μg/rat, intra-NAC) during conditioning. The preference score was calculated as the total time spent in the drug-paired chamber in post-conditioning day subtract the total time spent in the drug-paired chamber in pre-conditioning day.

2.7. Statistical analysis

Statistical Package for the Social Sciences (SPSS, Ver 25) was used for data analysis. Data were expressed as Means ± S.E.M. Using one-way and two-way analysis of variance (ANOVA) followed by Tukey Post hoc mean comparison test, all data were analyzed. A p-value lower than 0.05 was considered significant.

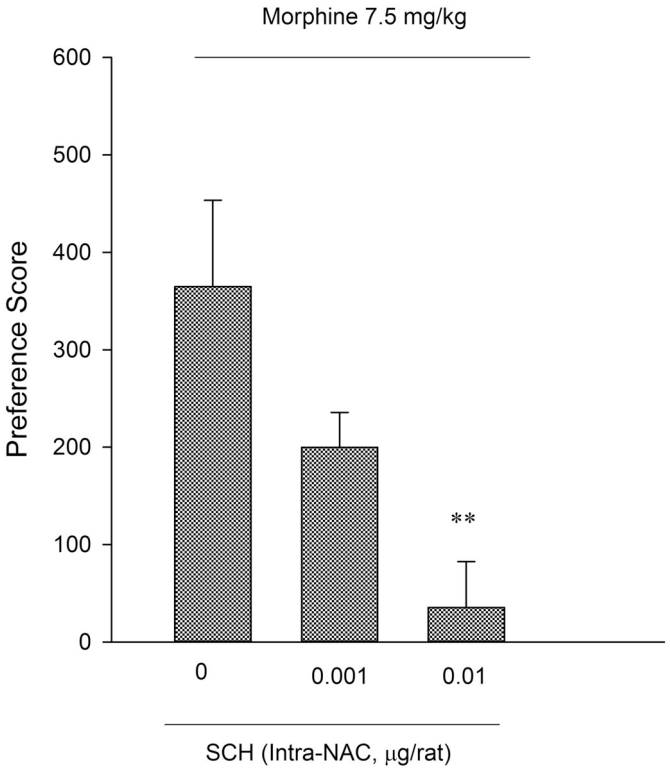

Fig. 2. Place preference produced by morphine was reversed dose-dependently by intra-NAC administration of SCH23390 (D1-like dopamine receptor antagonist). Morphine (7.5 mg/kg. Sc) was administrated in a three-day schedule of conditioning. During the conditioning phase, SCH in different doses (0, 0.01, and 0.001 μg/rat) was administrated intra-NAC. The difference score was assessed as a difference between time spent in the drug-paired compartment in testing and preconditioning day. Data are expressed as mean ± SEM for 8 rats in each group. $^{**}p < 0.01$.

3. Results

3.1. Intra-NAC administration of SCH inhibit conditioning induced by morphine

The dose-response of SCH in morphine CPP is shown in Fig. 2. The offspring of drug-naïve parents were used as the control group. The results of the analysis of variance (ANOVA) revealed that intra-NAC administration of SCH (0.01 μg/rat) could inhibit morphine-induced conditioning in the control groups ($F_{2,21} = 6.38$, $p = 0.008$).

3.2. Intra-NAC administration of SCH increase the rewarding effect of morphine in the offspring of morphine-abstinent rats

Fig. 3 shows the effect of intra-NAC administration of SCH (0.01 μg/rat) in morphine-induced CPP among groups. Analysis of the difference between the total time in the drug-paired chamber in the first and fifth day (two-way ANOVA) revealed that blocking of D1-like DR using SCH23390 in the NAC could potentiate morphine conditioning in the offspring of morphine-abstinent parents (inter group: $F_{3,56} = 0.99$, $p = 0.405$, intra group: $F_{1,56} = 4.39$, $p = 0.04$, and inter-intra group interaction: $F_{3,56} = 12.26$,$p < 0.001$).

4. Discussion

Previously we demonstrated that the offspring of morphine-abstinent parents did not condition with a high dose of morphine (7.5 mg/kg) in condition place preference paradigm [15]. Earlier data also revealed that prenatal morphine exposure induced morphine tolerance in the male offspring [37]. In addition, Chiang et al. [38] showed that prenatal morphine or methadone exposure developed tolerance to morphine in the offspring. Besides, changes in opioid receptor expression level induced tolerance in rats prenatally exposed to morphine [39,40]. It has been shown that the effect of morphine on up-regulation of the cAMP pathway [41], regulation of GABAergic and glutamatergic transmission, regulation of corticotropin-releasing factor (CRF) and VTA neuronal morphology lead to tolerance [42]. Furthermore, evidence indicated that morphine exposure during adolescence induced changes in the endogenous opioid system [43]. These changes might be transferred to the next generation and induced tolerance to the reinforcing effect of morphine in the offspring. Moreover, changes in the dopaminergic function might be induced alteration in the rewarding effect of morphine. It has been suggested that exposure of female rats to morphine before gestation increase the risk of substance abuse in the offspring [44] which dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis might be involved in these processes ([45–47]. All evidence might be referred to this issue that morphine exposure even before gestation affects morphine tolerance in the offspring.

In the current study, we revealed that D1-like DR located in the NAC might be involved in the tolerance induced by parental morphine-exposure. Our previous study revealed that D1-like DR upregulated in the NAC of the offspring of morphine-abstinent parents [48]. NAC received inputs from variable brain regions; glutamatergic input from the hippocampus, thalamus, amygdala, mesencephalon (VTA, SN pars compacta, retrorubral area), and PFC, dopaminergic inputs from VTA and SNpc, GABAergic inputs from mesencephalon (VTA, SN, A8), and pallidum, and other monoamines input (serotonin, acetylcholine, norepinephrine) from the brain stem (dorsal raphe nucleus, locus coeruleus, nucleus of the solitary tract, pedunculopontine nucleus) [49]. The output of the NAC comes from GABAergic medium spiny neurons (MSN) and projects to the mesencephalon, pallidum, basal ganglia, and hypothalamus [49]. It is well established that morphine increases dopamine release from VTA to the NAC [50] and enhances glutamate transmission in the NAC [51].

D1-like DR coupled with Gs and increases the phosphorylated-CREB, which leads to an increase in gene expression in the cell [17]. It is documented that D1-DR has a critical role in opioid reward and reinforcement and is correlated to the relapse process in morphine addiction [52–54]. Moreover, D1-like DR plays a significant role in the development of morphine dependence [55]. In addition, the role of D1-like DR in morphine tolerance was investigated using optogenetic studies [56]. There are also studies indicated that D1 blockade in the NAC decreases alcohol-seeking behavior [57] and heroin intake [58]. Moreover, it has been shown that activation of dopamine D1-MSN accelerates the development of tolerance via enhancing the level of Regulator of G protein Signaling 9 (RGS9) in the NAC [56]. D1-DR in the NAC is a limiting response agent in NAC-VTA pathway [30]. It is well established that the direct projection from NAC to VTA is composed of D1-MSN [59–61]. Then it is speculated that activation of D1-like DR leads to increase GABA release in the VTA and inhibit dopamine release into the NAC. It is in agreement with the current results indicated that morphine-induced conditioning (preference score) was decreased after intra-NAC administration of SCH23390 – as a D1-like DR antagonist – in the drug-naïve offspring.

The current investigation indicated that intra accumbal administration of SCH23390 in the offspring of morphine-abstinent parents caused to increase preference score in morphine-induced CPP paradigm. Previously, we found that D1-like DR [48], opioid receptors (μ, κ, and δ), p-CREB and p-ERK [16] enhanced in the NAC of the offspring of morphine-abstinent parents. As mentioned before, morphine tolerance was developed in the offspring of morphine abstinent parents [15]. “Cyclic AMP hypothesis” is one of the oldest hypothesis for the mechanisms underlying morphine tolerance [62,63]. It has been shown that increases CREB expression in the NAC decreases the reward properties of morphine [64,65]. Moreover, the elevation in the level of

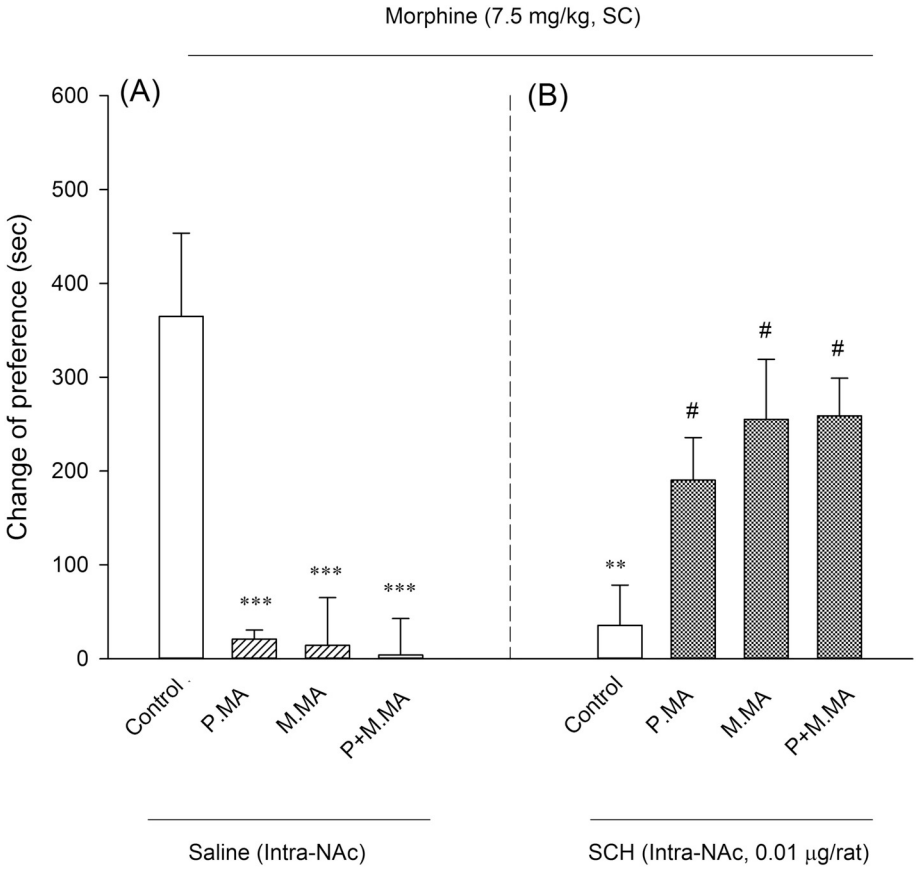

Fig. 3. (A) Morphine administration in a high dose (7.5 mg/kg) does not induce conditioning in the offspring of morphine-exposed parent(s). (B) Administration of SCH23390 (0.01 μg/rat) intra-NAC increase preference score in the offspring of morphine-abstinent parents. M.ME: maternal morphine exposed offspring, P.ME: paternal morphine-exposed offspring. Data are expressed as mean ± SEM. ***$p < 0.001$ different from the control group. #$p < 0.05$ difference from saline-treated morphine-abstinent offspring.

p-CREB in the NAC was observed after morphine-induced conditioning [66]. Recent data show that reducing the activation of ERK/CREB signaling using microRNA alleviated morphine-induced tolerance [67]. Since, increasing in D1-like DR signaling enhanced drug reward [68] and according to this fact that activation of D1-like DR signaling increase p-CREB, thus decreasing p-CREB level using D1-like DR antagonist might be involved in the response of the offspring of morphine-abstinent parents to the morphine-induced conditioning. Then it is speculated that tolerance induced by parental morphine-exposure might be diminished by blocking of D1-like DR located in the NAC.

It is not doubtable that other receptors and signaling pathways are involved in the tolerance process. It needs further studies to find all the changes induced by parental morphine exposure.

5. Conclusion

The results of the current investigation revealed that NAC D1-like DR blockade dose-dependently inhibits morphine-induced conditioning in the rats. Also, intra-NAC administration of SCH23390 increased the reinforcing effect of morphine in the litter of morphine-abstinent parent (s). Then it might suggest that dysregulation of D1-like DR located in the NAC in the offspring of morphine-abstinent parents might be involved in morphine tolerance in the CPP paradigm. Since activation of D1-DR increased the p-CREB level in the cell, then the changes in p-CREB level might be involved in the tolerance induced by parental morphine exposure.

Declaration of competing interest

Authors declare no conflict of interest.

Acknowledgments

We would like to show our gratitude to Faran Shimi Company for providing morphine sulfate for this study.

References

[1] E. Kalso, J.E. Edwards, R.A. Moore, H.J. McQuay, Opioids in chronic non-cancer pain: systematic review of efficacy and safety, Pain 112 (2004) 372–380.
[2] R. Miech, L. Johnston, P.M. O'Malley, K.M. Keyes, K. Heard, Prescription opioids in adolescence and future opioid misuse, Pediatrics 136 (2015) e1169–e1177.
[3] A. Badiani, T.E. Robinson, Drug-induced neurobehavioral plasticity: the role of environmental context, Behav. Pharmacol. 15 (2004) 327–339.
[4] M.A. Enoch, The influence of gene-environment interactions on the development of alcoholism and drug dependence, Current Psychiatry Reports 14 (2012) 150–158.
[5] D.A. Nielsen, M.J. Kreek, Common and specific liability to addiction: approaches to association studies of opioid addiction, Drug Alcohol Depend. 123 (Suppl. 1) (2012) S33–S41.
[6] A. Fodor, J. Timar, D. Zelena, Behavioral effects of perinatal opioid exposure, Life Sci. 104 (2014) 1–8.
[7] R. Gabrhelik, B. Nechanska, V. Mravcik, S. Skurtveit, I.O. Lund, M. Handal, A unique opportunity to study short and long term consequences in children prenatally exposed to illicit drugs and opioid maintenance treatment using Czech and Scandinavian registers, Cent. Eur. J. Public Health 24 (2016) 248–251.
[8] N.D. Volkow, J.S. Fowler, G.J. Wang, The addicted human brain: insights from imaging studies, J. Clin. Invest. 111 (2003) 1444–1451.
[9] J.M. Mitchell, J.P. O'Neil, M. Janabi, S.M. Marks, W.J. Jagust, H.L. Fields, Alcohol consumption induces endogenous opioid release in the human orbitofrontal cortex and nucleus accumbens, Sci. Transl. Med. 4 (2012) 116ra6.
[10] N.D. Volkow, G.J. Wang, F. Telang, J.S. Fowler, J. Logan, M. Jayne, et al., Profound decreases in dopamine release in striatum in detoxified alcoholics: possible orbitofrontal involvement, J. Neurosci. 27 (2007) 12700–12706.
[11] G. Di Chiara, A. Imperato, Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats, Proc. Natl. Acad. Sci. U. S. A. 85 (1988) 5274–5278.
[12] G.F. Koob, N.R. Swerdlow, The functional output of the mesolimbic dopamine system, Ann. N. Y. Acad. Sci. 537 (1988) 216–227.
[13] T.P. Piepponen, A. Honkanen, T. Kivastik, A. Zharkovsky, A. Turtia, J.A. Mikkola, et al., Involvement of opioid mu1-receptors in opioid-induced acceleration of striatal and limbic dopaminergic transmission, Pharmacol. Biochem. Behav. 63 (1999) 245–252.

[14] P.L. Wood, T.S. Rao, Morphine stimulation of mesolimbic and mesocortical but not nigrostriatal dopamine release in the rat as reflected by changes in 3-methoxytyramine levels, Neuropharmacology 30 (1991) 399–401.
[15] M.S. Sadat-Shirazi, F. Karimi, G. Kaka, G. Ashabi, I. Ahmadi, A. Akbarabadi, et al., Parental morphine exposure enhances morphine (but not methamphetamine) preference and increases monoamine oxidase-B level in the nucleus accumbens, Behav. Pharmacol. 30 (5) (2019) 435–445.
[16] G. Ashabi, M.S. Sadat-Shirazi, A. Akbarabadi, N. Vousooghi, Z. Kheiri, H. Toolee, et al., Is the nociception mechanism altered in offspring of morphine-abstinent rats? The Journal of Pain 19 (2018) 529–541.
[17] J.M. Beaulieu, R.R. Gainetdinov, The physiology, signaling, and pharmacology of dopamine receptors, Pharmacol. Rev. 63 (2011) 182–217.
[18] Z. Luo, N.D. Volkow, N. Heintz, Y. Pan, C. Du, Acute cocaine induces fast activation of D1 receptor and progressive deactivation of D2 receptor striatal neurons: in vivo optical microprobe $[Ca^{2+}]_i$ imaging, J. Neurosci. 31 (2011) 13180–13190.
[19] J.G. Parker, L.S. Zweifel, J.J. Clark, S.B. Evans, P.E. Phillips, R.D. Palmiter, Absence of NMDA receptors in dopamine neurons attenuates dopamine release but not conditioned approach during Pavlovian conditioning, Proc. Natl. Acad. Sci. U. S. A. 107 (2010) 13491–13496.
[20] D.J. Surmeier, W. Shen, M. Day, T. Gertler, S. Chan, X. Tian, et al., The role of dopamine in modulating the structure and function of striatal circuits, Prog. Brain Res. 183 (2010) 149–167.
[21] A.J. Robison, E.J. Nestler, Transcriptional and epigenetic mechanisms of addiction, Nat. Rev. Neurosci. 12 (2011) 623–637.
[22] J.A. Garcia-Sevilla, M. Ferrer-Alcon, M. Martin, B.L. Kieffer, R. Maldonado, Neurofilament proteins and cAMP pathway in brains of mu-, delta- or kappa-opioid receptor gene knock-out mice: effects of chronic morphine administration, Neuropharmacology 46 (2004) 519–530.
[23] Y. Chen, C. Sommer, The role of mitogen-activated protein kinase (MAPK) in morphine tolerance and dependence, Mol. Neurobiol. 40 (2009) 101–107.
[24] A. Akbarabadi, S. Niknamfar, N. Vousooghi, M.S. Sadat-Shirazi, H. Toolee, M.R. Zarrindast, Effect of rat parental morphine exposure on passive avoidance memory and morphine conditioned place preference in male offspring, Physiol. Behav. 184 (2018) 143–149.
[25] S. Sabzevari, K. Rohbani, M.S. Sadat-Shirazi, N. Babhadi-Ashar, A. Shakeri, G. Ashabi, et al., Morphine exposure before conception affects anxiety-like behavior and CRF level (in the CSF and plasma) in the adult male offspring, Brain Res. Bull. 144 (2019) 122–131.
[26] F.M. Vassoler, A.M. Toorie, E.M. Byrnes, Transgenerational blunting of morphine-induced corticosterone secretion is associated with dysregulated gene expression in male offspring, Brain Res. 1679 (2018) 19–25.
[27] M.T. Bardo, J.K. Rowlett, M.J. Harris, Conditioned place preference using opiate and stimulant drugs: a meta-analysis, Neurosci. Biobehav. Rev. 19 (1995) 39–51.
[28] J.E. Zadina, A.J. Kastin, D.H. Coy, B.A. Adinoff, Developmental, behavioral, and opiate receptor changes after prenatal or postnatal beta-endorphin, CRF, or Tyr-MIF-1, Psychoneuroendocrinology 10 (1985) 367–383.
[29] Y.Y. Ma, L. Meng, C.Y. Guo, J.S. Han, D.Y. Lee, C.L. Cui, Dose- and time-dependent, context-induced elevation of dopamine and its metabolites in the nucleus accumbens of morphine-induced CPP rats, Behav. Brain Res. 204 (2009) 192–199.
[30] L. Sun, L. Hu, Y. Li, C. Cui, Mesoaccumbens dopamine signaling alteration underlies behavioral transition from tolerance to sensitization to morphine rewarding properties during morphine withdrawal, Brain Struct. Funct. 219 (2014) 1755–1771.
[31] G. Paxinos, C. Watson, The Rat Brain in Stereotaxic Coordinates, Elsevier Academic Press, 2005.
[32] D.C. Hoffman, The use of place conditioning in studying the neuropharmacology of drug reinforcement, Brain Res. Bull. 23 (1989) 373–387.
[33] C. Chen, Z. Nong, X. Liang, M. Meng, F. Xuan, Q. Xie, et al., Effect of Yulangsan polysaccharide on the reinstatement of morphine-induced conditioned place preference in Sprague-Dawley rats, Neurochem. Res. 43 (2018) 918–929.
[34] J.R. Markos, H.M. Harris, W. Gul, M.A. ElSohly, K.J. Sufka, Effects of cannabidiol on morphine conditioned place preference in mice, Planta Med. 84 (2018) 221–224.
[35] M. Nasehi, L. Kamali-Dolatabadi, M. Torabi-Nami, M.R. Zarrindast, Possible involvement of the CA1 GABAA receptors upon acquisition and expression of the ACPA-induced place preference in mice, Physiol. Behav. 161 (2016) 155–165.
[36] M.R. Zarrindast, M. Ebrahimi-Ghiri, P. Rostami, A. Rezayof, Repeated pre-exposure to morphine into the ventral pallidum enhances morphine-induced place preference: involvement of dopaminergic and opioidergic mechanisms, Behav. Brain Res. 181 (2007) 35–41.
[37] G.C. Wagner, M.F. Jarvis, D.S. Gottesfeld, M. Giorlando, J. Rabii, The effects of prenatal morphine on the responsiveness to morphine and amphetamine, Pharmacol. Biochem. Behav. 24 (1986) 757–759.
[38] Y.C. Chiang, T.W. Hung, C.W. Lee, J.Y. Yan, I.K. Ho, Enhancement of tolerance development to morphine in rats prenatally exposed to morphine, methadone, and buprenorphine, J. Biomed. Sci. 17 (2010) 46.
[39] R. Bhat, G. Chari, R. Rao, Effects of prenatal cocaine, morphine, or both on postnatal opioid (mu) receptor development, Life Sci. 78 (2006) 1478–1482.
[40] A. Rimanoczy, I. Vathy, Prenatal exposure to morphine alters brain mu opioid receptor characteristics in rats, Brain Res. 690 (1995) 245–248.
[41] T.J. De Vries, B.J. Van Vliet, F. Hogenboom, G. Wardeh, J.W. Van der Laan, A.H. Mulder, et al., Effect of chronic prenatal morphine treatment of mu-opioid receptor-regulated adenylate cyclase activity and neurotransmitter release in rat brain slices, Eur. J. Pharmacol. 208 (1991) 97–104.
[42] E.J. Nestler, S.E. Hyman, R.C. Malenka, Molecular Neuropharmacology: A Foundation for Clinical Neuroscience, Third edition, McGraw-Hill Education, 2015.
[43] E.M. Byrnes, Chronic morphine exposure during puberty induces long-lasting changes in opioid-related mRNA expression in the mediobasal hypothalamus, Brain Res. 1190 (2008) 186–192.
[44] F.M. Vassoler, E.M. Byrnes, R.C. Pierce, The impact of exposure to addictive drugs on future generations: physiological and behavioral effects, Neuropharmacology 76 (Pt B) (2014) 269–275.
[45] E.M. Byrnes, Transgenerational consequences of adolescent morphine exposure in female rats: effects on anxiety-like behaviors and morphine sensitization in adult offspring, Psychopharmacology 182 (2005) 537–544.
[46] J.J. Byrnes, J.A. Babb, V.F. Scanlan, E.M. Byrnes, Adolescent opioid exposure in female rats: transgenerational effects on morphine analgesia and anxiety-like behavior in adult offspring, Behav. Brain Res. 218 (2011) 200–205.
[47] T.J. Cicero, M.L. Adams, A. Giordano, B.T. Miller, L. O'Connor, B. Nock, Influence of morphine exposure during adolescence on the sexual maturation of male rats and the development of their offspring, J. Pharmacol. Exp. Ther. 256 (1991) 1086–1093.
[48] N. Vousooghi, M.S. Sadat-Shirazi, P. Safavi, R. Zeraati, A. Akbarabadi, S.M. Makki, et al., Adult rat morphine exposure changes morphine preference, anxiety, and the brain expression of dopamine receptors in male offspring, International Journal of Developmental Neuroscience 69 (2018) 49–59.
[49] R. Splittgerber, Snell's Clinical Neuroanatomy, Lippincott Williams & Wilkins, 2018.
[50] E.J. Nestler, Is there a common molecular pathway for addiction? Nat. Neurosci. 8 (2005) 1445–1449.
[51] K. Yuan, H. Sheng, J. Song, L. Yang, D. Cui, Q. Ma, et al., Morphine treatment enhances glutamatergic input onto neurons of the nucleus accumbens via both disinhibitory and stimulating effect, Addict. Biol. 22 (2017) 1756–1767.
[52] J.T. Dudman, M.E. Eaton, A. Rajadhyaksha, W. Macias, M. Taher, A. Barczak, et al., Dopamine D1 receptors mediate CREB phosphorylation via phosphorylation of the NMDA receptor at Ser897-NR1, J. Neurochem. 87 (2003) 922–934.
[53] D.L. Muller, E.M. Unterwald, D1 dopamine receptors modulate deltaFosB induction in rat striatum after intermittent morphine administration, J. Pharmacol. Exp. Ther. 314 (2005) 148–154.
[54] V. Zachariou, C.A. Bolanos, D.E. Selley, D. Theobald, M.P. Cassidy, M.B. Kelz, et al., An essential role for DeltaFosB in the nucleus accumbens in morphine action, Nat. Neurosci. 9 (2006) 205–211.
[55] F. Zhu, C.X. Yan, Y.C. Wen, J. Wang, J. Bi, Y.L. Zhao, et al., Dopamine D1 receptor gene variation modulates opioid dependence risk by affecting transition to addiction, PLoS One 8 (2013) e70805.
[56] S. Gaspari, M.M. Papachatzaki, J.W. Koo, F.B. Carr, M.E. Tsimpanouli, E. Stergiou, et al., Nucleus accumbens-specific interventions in RGS9-2 activity modulate responses to morphine, Neuropsychopharmacology 39 (2014) 1968–1977.
[57] A.S. Hamlin, J. Newby, G.P. McNally, The neural correlates and role of D1 dopamine receptors in renewal of extinguished alcohol-seeking, Neuroscience 146 (2007) 525–536.
[58] M.A. Gerrits, N.F. Ramsey, G. Wolterink, J.M. van Ree, Lack of evidence for an involvement of nucleus accumbens dopamine D1 receptors in the initiation of heroin self-administration in the rat, Psychopharmacology 114 (1994) 486–494.
[59] C. Bocklisch, V. Pascoli, J.C. Wong, D.R. House, C. Yvon, M. de Roo, et al., Cocaine disinhibits dopamine neurons by potentiation of GABA transmission in the ventral tegmental area, Science 341 (2013) 1521–1525.
[60] Y.M. Kupchik, R.M. Brown, J.A. Heinsbroek, M.K. Lobo, D.J. Schwartz, P.W. Kalivas, Coding the direct/indirect pathways by D1 and D2 receptors is not valid for accumbens projections, Nat. Neurosci. 18 (2015) 1230–1232.
[61] M. Watabe-Uchida, L. Zhu, S.K. Ogawa, A. Vamanrao, N. Uchida, Whole-brain mapping of direct inputs to midbrain dopamine neurons, Neuron 74 (2012) 858–873.
[62] H.O. Collier, D.L. Francis, Morphine abstinence is associated with increased brain cyclic AMP, Nature 255 (1975) 159–162.
[63] S.K. Sharma, W.A. Klee, M. Nirenberg, Dual regulation of adenylate cyclase accounts for narcotic dependence and tolerance, Proc. Natl. Acad. Sci. U. S. A. 72 (1975) 3092–3096.
[64] M. Barrot, J.D. Olivier, L.I. Perrotti, R.J. DiLeone, O. Berton, A.J. Eisch, et al., CREB activity in the nucleus accumbens shell controls gating of behavioral responses to emotional stimuli, Proc. Natl. Acad. Sci. U. S. A. 99 (2002) 11435–11440.
[65] T.Z. Shaw-Lutchman, M. Barrot, T. Wallace, L. Gilden, V. Zachariou, S. Impey, et al., Regional and cellular mapping of cAMP response element-mediated transcription during naltrexone-precipitated morphine withdrawal, J. Neurosci. 22 (2002) 3663–3672.
[66] J.A. Moron, S. Gullapalli, C. Taylor, A. Gupta, I. Gomes, L.A. Devi, Modulation of opiate-related signaling molecules in morphine-dependent conditioned behavior: conditioned place preference to morphine induces CREB phosphorylation, Neuropsychopharmacology 35 (2010) 955–966.
[67] X.P. Wu, R.X. She, Y.P. Yang, Z.M. Xing, H.W. Chen, Y.W. Zhang, MicroRNA-365 alleviates morphine analgesic tolerance via the inactivation of the ERK/CREB signaling pathway by negatively targeting beta-arrestin2, J. Biomed. Sci. 25 (2018) 10.
[68] M.K. Lobo, E.J. Nestler, The striatal balancing act in drug addiction: distinct roles of direct and indirect pathway medium spiny neurons, Front. Neuroanat. 5 (2011) 41.