

## 5-HT<sub>1A</sub>

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### Evaluation of the role of 5-HT<sub>1A</sub> receptors in Dorsal and Median raphe nuclei on the morphine withdrawal syndrome in rat

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**OBJECTIVES:** The present study was performed to investigate the role of 5-HT<sub>1A</sub> receptors in dorsal and median raphe nuclei on the withdrawal syndrome of morphine and acceleration the restraint of opioides. **METHODS:** Experiments were performed on adult male wistar rats weighing between 225 and 275 g. The control group (n=8) had 9 days s.c. injections of morphine (5, 10, 10, 15, 15, 20, 20, 25, 25mg/kg/12h) and the last day, 60 minutes after first injection of morphine, 5mg/kg naloxone was injected (i.p.) and signs of withdrawal syndrome were recorded until 60 minutes. In the sham and test groups following induction anesthesia, rats were secured in a stereotaxic frame with ear and incisor bars. Then a guide cannula was implanted into the DRN and MRN in the separated groups (n=8). After five days recovery of animals, injections of morphine began and the 9<sup>th</sup> day, 55 minutes after first s.c. injection of morphine, 1μl/2min of 1-(2-methoxyphenyl)-4-[4-(2-phthalimido) butyl]piperazine hydrobromide (NAN-190) vehicle was injected into the nuclei in the sham group. But in the test groups, 1.5, 3.0 and 6.0 μg/μl/2min of NAN-190 (antagonist of 5-HT<sub>1A</sub> receptors) was injected into the nuclei, and then naloxone was injected (i.p.). **RESULTS:** Data signs were analyzed by one way ANOVA and Tukey post test. The results of this study showed a significant decrease in some of the recorded morphine withdrawal signs (jumping p<0.05, writhing p<0.01 and wet-dog shakes p<0.001) in test groups in comparison with the control group. **CONCLUSION:** The results confirmed the important role of 5-HT<sub>1A</sub> receptors in raphe nucleuses on some of the morphine withdrawal signs and may dissolve problems of opioides addiction.

**Key words:** 5-HT<sub>1A</sub> receptors, Dorsal raphe nucleus, Median raphe nucleus, Morphine, Withdrawal syndrome.

(MRN) (DRN)  
(n=8)  
5 mg/kg (mg/kg/12h)  
MRN DRN sham  
NAN-190 / / / μg/μl/2min  
Tukey one way ANOVA  
p<0.001 p<0.01 p<0.05  
1 μl/2min (NAN-190) ( [ ( ) ] ( )  
sham  
(5-HT<sub>1A</sub>)  
NAN-190 ( )  
5-HT<sub>1A</sub>  
5-HT<sub>1A</sub>

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Ph.D

SSRIs

( )

DRN

( )

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( )

(NAN-190) 5-HT<sub>1A</sub>

5-HT<sub>1A</sub>

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( ± )

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(PAG

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(NAN-190) (

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(Sigma, St.Louis, MO)

(

)

(Sigma, St.Louis, MO) (8-OH-DPAT) [

(TEMAD CO., Tehran, Iran)

(Kela n.v., Hoogstraten, Belgium)

( )

( )

(% / )

( )

1- SSRIs = Serotonin Specific Reuptake Inhibitors

2- DRN: Dorsal Raphe Nucleus

( )

( ) NAN-190

mg/kg

NAN-190 ( )

( $\mu\text{g}/\mu\text{l}/2\text{min}$  / / / ) DRN

( ) V: -7.4<sup>mm</sup> L:  $\pm$  4.0<sup>mm</sup> AP: - 7.64<sup>mm</sup>

NAN-19 V: -9.0<sup>mm</sup> L:  $\pm$  4.0<sup>mm</sup> AP: - 7.64<sup>mm</sup> MRN<sup>3</sup>

AP) L V

( ) 8 $\mu\text{g}$  (8-OH-DPAT) 5-HT<sub>1A</sub>

NAN-190 ( ) MRN 10<sup>mm</sup> DRN 8<sup>mm</sup>

(MRN DRN)

8 $\mu\text{g}/\mu\text{l}/2\text{min}$

NAN-190 6 $\mu\text{g}/\mu\text{l}/2\text{min}$  8-OH-DPAT

%

( mg/ml)

(mg/kg/12h

( )

5 mg/kg

(

wet-dog shakes abdomen writhing (jumping)

( genital grooming teeth chattering (wet-dogshakes)

(teeth chattering) (abdomen writhing)

(genital grooming)

One way ANOVA t-test

P<0.05 . Tukey

(.ml/kg/12h / / / / / / / / / )

(NAN-190 )

NAN-190 1 $\mu\text{l}/2\text{min}$



3- MRN: Median Raphe Nucleus





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( )

5-HT<sub>1</sub> (up-regulation) :  
5-HT<sub>1</sub> ( )  
( ) 5-HT<sub>2</sub>

( )

5-HT<sub>1A</sub>  
DRN NAN-190

quipazine ( )

MRN ( )

NAN-190

DRN  
5-HT<sub>1A</sub>

MRN ( ) 5-HT<sub>1A</sub>

5-HT<sub>1A</sub>

DRN 5-HT<sub>1A</sub> MRN DRN

(NAN-190) (8-OH-DPAT) 5-HT<sub>1A</sub>

( ) 5-HT<sub>1A</sub>

D<sub>2</sub> ( )

α<sub>1</sub>

( )

8-OH-DPAT NAN-190

NAN-190

( )

( 5-HT<sub>1A</sub>  
5-HT<sub>1A</sub>

5-HT<sub>1A</sub>

( ) (SSRIs

5-HT<sub>2</sub>

5-HT<sub>1A</sub>

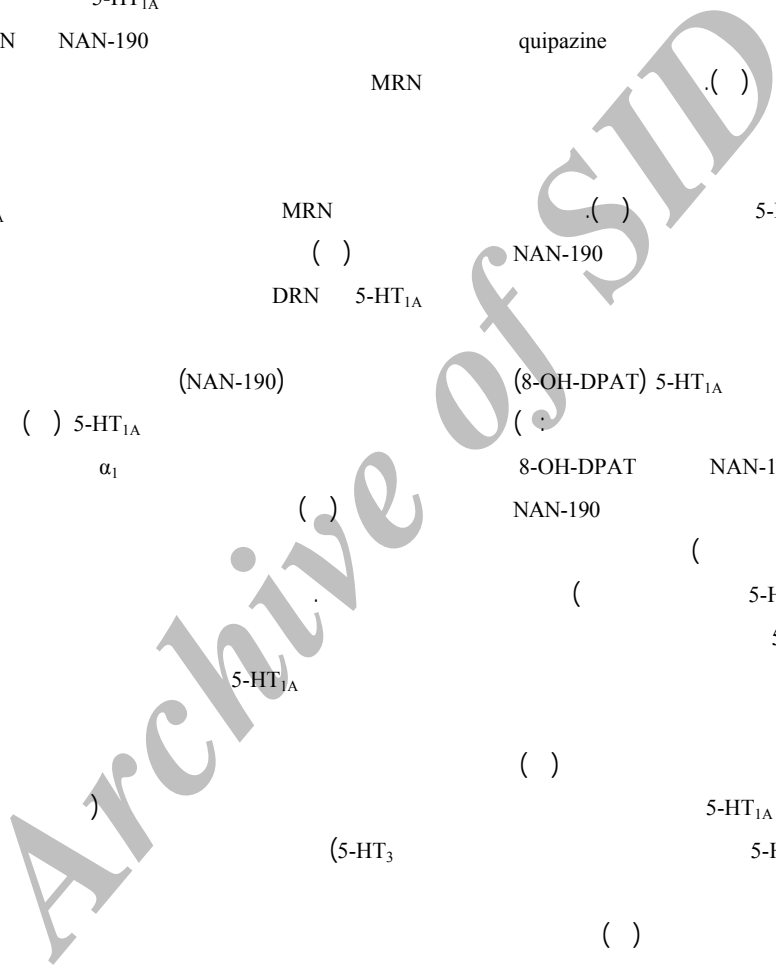
(5-HT<sub>3</sub>

5-HT<sub>1A</sub>

up-regulation

( )

5-HT<sub>1A</sub>



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