

5-HT<sub>2</sub>

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## Evaluation of the role of 5-HT<sub>2</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>2</sub> receptors in dorsal and median raphe nuclei on the withdrawal syndrome of morphine and accelerated the restraint of opioids. **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 for 60 minutes. In the sham and test groups 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 α-Me-5HT vehicle was injected into the nuclei in the sham group. But in the test groups, 2.5, 5.0 and 10.0 μg/μl/2min of α-Me-5HT (agonist of 5-HT<sub>2</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 (for example for highest dose of α-Me-5HT in DRN: jumping p<0.05, teeth chattering p<0.01, wet-dog shakes p<0.001 and genital grooming p<0.05) in test groups in comparisons with the control group. **Conclusion:** The results confirmed the important role of 5-HT<sub>2</sub> receptors in raphe nucleuses on some of the morphine withdrawal signs and may dissolve problems of opioids addiction.

**Key words:** 5-HT<sub>2</sub> receptors, Dorsal raphe nucleus, Median raphe nucleus, Morphine, Withdrawal syndrome.

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

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( mg/ml) :

(mg/kg/12h )

( )

( ° ± )

mg/kg :

( )

(jumping) J

(wet-dog shakes) WDS

(teeth chattering) TC (abdomen writhing) AW :

(genital grooming) GG

(Sigma, St. Louis, MO) (α-Me-5HT)

(TEMAD CO., Tehran, Iran)

(mg/kg/12h ) (Kela n.v., Hoogstraten, Belgium)

( )

( mg/kg) (% / )

α-Me-5HT

( sham)

(ml/kg/12h / / / / / / / / / ) mg/kg

(α-Me-5HT )

α-Me-5HT μl/2min ( )

DRN

V: -7.4<sup>mm</sup> L: ± 4.0<sup>mm</sup> AP: - 7.64<sup>mm</sup>

V: -9.0<sup>mm</sup> L: ± 4.0<sup>mm</sup> AP: - 7.64<sup>mm</sup> MRN<sup>1</sup>

AP)

α-Me-5HT L

( mm V

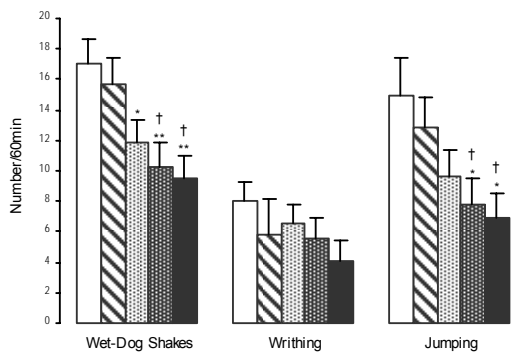
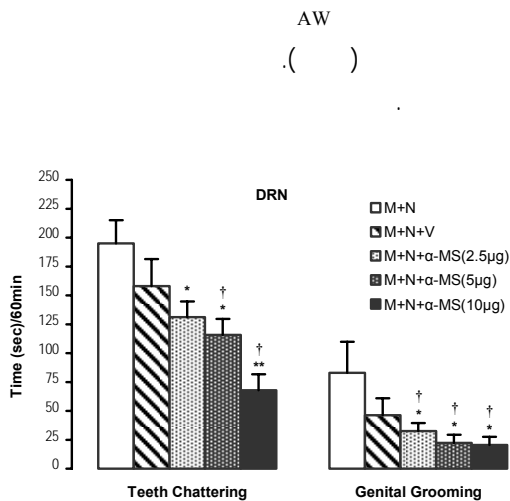
(μg/μl/2min / / / ) α-Me-5HT

( ) MRN mm DRN

%

% :

1- MRN: Median Raphe Nucleus



(.5mg/kg, i.p.)  
(n=6-8) mean+S.E.M.  
(M+N)  
(M+N+V) sham (\*\*\*P<0.001 \*\*P<0.01 \*P<0.05)  
(†††P<0.001 ††P<0.01 †P<0.05)  
M=Morphine, N=Naloxone, V=Vehicle

Tukey one way ANOVA  
P<0.05

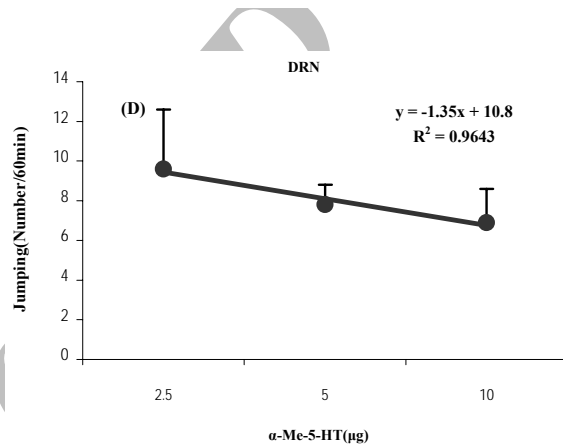
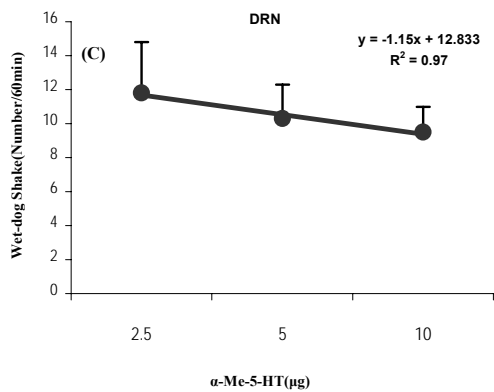
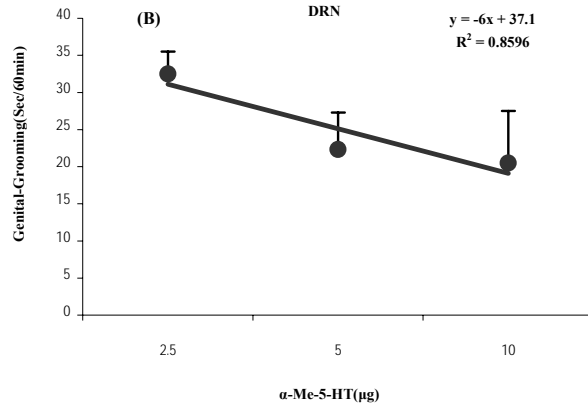
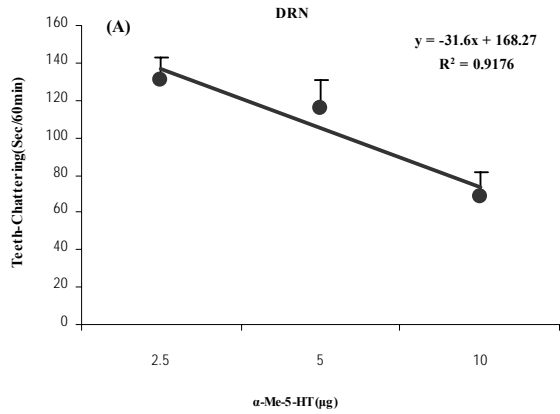
(p<0.001)

α-Me-5HT

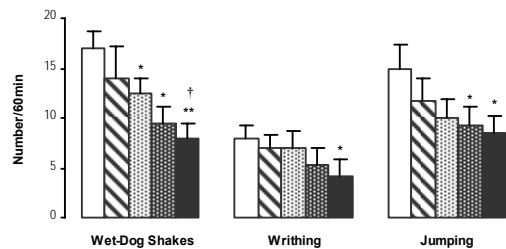
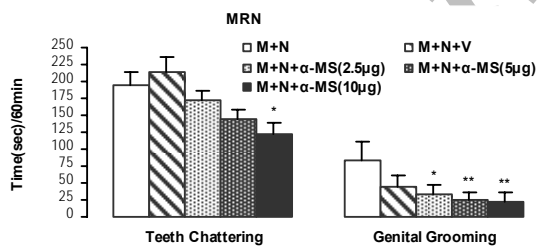
sham  
(α-Me-5HT / / / μg/μl/2min  
WDS J

sham )  
GG TC

F<sub>(7,15)</sub>=9.0, p<0.05; α-Me-5HT  
F<sub>(7,13)</sub>=15.562 p<0.01 WDS F<sub>(7,15)</sub>=17.632, p<0.01 J  
GG F<sub>(7,13)</sub>=5.725, p<0.05 TC  
F<sub>(7,13)</sub>=7.532, p<0.05 J F<sub>(7,13)</sub>=6.836, p<0.05 :sham  
(GG F<sub>(7,13)</sub>=6.542, p<0.05 TC F<sub>(7,13)</sub>=8.561 p<0.05 WDS



(A) (B) (C) (D)  $\alpha$ -Me-5HT : MRN



(A) (B)  $\alpha$ -Me-5HT : MRN  
(.5mg/kg,i.p.)

(n=6-8) mean+S.E.M.  
 (\*\*\*)P<0.001 (\*\*\*)P<0.01 (\*)P<0.05 (M+N)  
 (†††)P<0.001 (††)P<0.01 (†)P<0.05 (M+N+V) sham  
 M=Morphine, N=Naloxone, V=Vehicle.

$\alpha$ -Me-5HT : MRN  
 MRN  
 WDS J  
 GG  
 sham  
 )  
 $F_{(7,14)}=7.571, p<0.05$  :  $\alpha$ -Me-5HT  
 $F_{(7,12)}=6.572, p<0.05$  WDS  $F_{(7,14)}=17.451, p<0.01$  J  
 GG  $F_{(7,14)}=15.762, p<0.01$  TC  
 (TC  $F_{(7,14)}=13.573, p<0.01$  :sham  
 AW  
 ( )

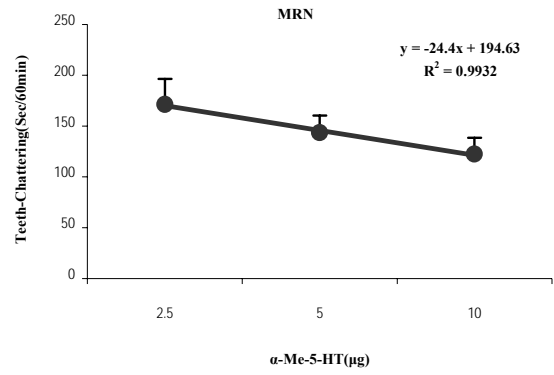
5-HT<sub>2</sub>

( )

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5-HT<sub>2</sub>

( )



α

( )

5-HT<sub>2A</sub>

5-HT<sub>2</sub>

( )

5-HT<sub>2A</sub>

(5-HT<sub>2</sub>

) α-Me-5HT

5-HT<sub>2</sub>

DRN

MRN

TC GG WDS J

TC

(sham)

PAG

(DRN )

( )

( )

μ

5-HT<sub>2</sub>

( )

( )

( )

( )

5-HT<sub>2</sub>

) SSRIs

5-HT<sub>2</sub>

(

) SSRI<sub>s</sub>

( ( )

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