

Descending serotonergic inhibition with dominant role of spinal 5-HT1A receptor in late-phase allodynia in carrageenan-induced inflammatory pain.

J.H. Yang, J.I. Choi, Dept of Anesthesiology and Pain Medicine, Chonnam National University, Gwangju, Korea

Introduction

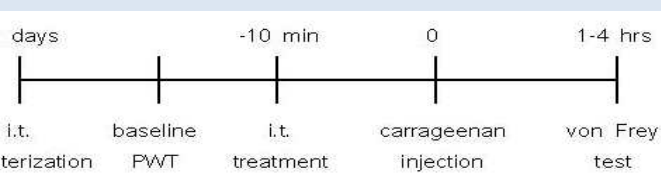
Physiological studies demonstrated a limited role of 5-hydroxytryptamine 3 receptor (5-HT₃), but facilitatory role of 5-HT_{1A}R and 5-HT_{1B}R in spinal nociceptive processing of carrageenan-induced inflammatory pain. Serotonin (5-hydroxytryptamine, 5-HT) release in spinal cord reaches the maximum 2-3 hours and returns to baseline 8 hours after carrageenan injection, indicating a different role of spinal serotonergic projection neurons between early- and late-phase of carrageenan inflammation.

Materials and Methods

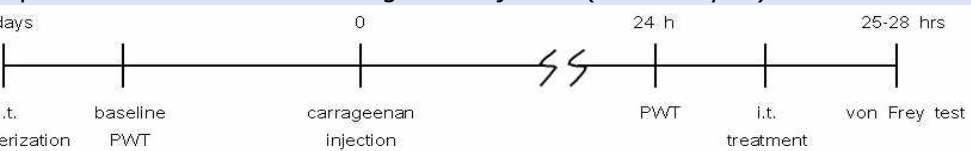
SD rats, intrathecal (i.t.) catheterization, von Frey test

5-HT hydrochloride, 8-OH-DPAT (5-HT_{1A} agonist), CP93129 (5-HT_{1B} agonist), mCPBG (5-HT_{1C} agonist), WAY-100635 (5-HT_{1A}R), SB-224289 (5-HT_{1B}R), Ondansetron (5-HT_{3R})

Experiment – Immediately after carrageenan injection (Early allodynia)



Experiment –24 hours after carrageenan injection (Late allodynia)



Experiment – Effect of i.t. 5-HT in normal or 5-HT depleted rat

5,7-dihydroxytryptamine (5,7-DHT, 60µl/20ml) 3 days before

intrathecal injection of carrageenan for 5-HT depletion

HPLC and HPLC-MS/MS for HPLC and HPLC-MS/MS of spinal 5-HT content

Maximum possible effect or hyperalgesic area under curve was calculated for the statistical analysis.

Results

Fig. 1. 5-HT (serotonin) of anti-allodynic effect in early and late-phase allodynia.

5-HT; No significant effect on early allodynia, but attenuated the late allodynia

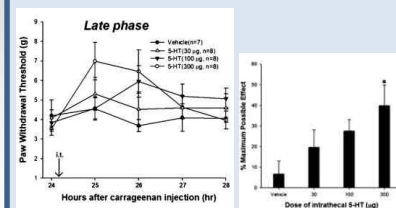


Fig. 2. Effect of i.t. 5-HT on enhanced allodynia in 5-DHT depleted rat.

Both early and late allodynia enhanced.

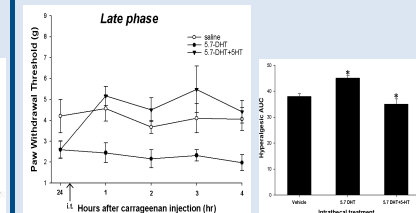
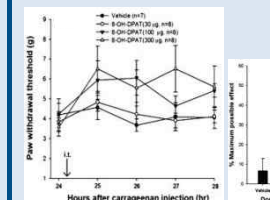


Fig. 3. 5-HT_{1A}R agonist (8-OH-DPAT) produce significant anti-allodynic effect on late-phase allodynia.

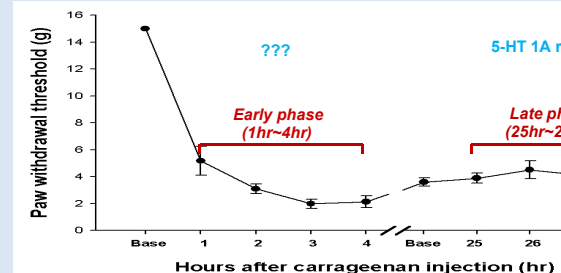
8-OH-DPAT; No significant effect on early allodynia, but attenuated the late allodynia



Conclusions

❖ Spinal 5-HT_{1A}, but not 5-HT_{1B}, 5-HT₃, receptors mediate the descending serotonergic inhibition on spinal nociceptive processing of late-phase mechanical allodynia in carrageenan induced inflammation.

❖ Descending serotonergic inhibition role in carrageenan-induced late-phase allodynia



References

- [1] S. Bingham, P.T. Davey, M. Sammons, P. Raval, P. Overend, A.A. Parsons, Inhibition of inflammatory-induced thermal hypersensitivity by sumatriptan through activation of 5-HT_{1B/1D} receptors, *Exp. Neurol.* 167 (2001) 65–73.
- [2] C.O. Asante, A.H. Dickenson, Descending serotonergic facilitation mediated by spinal 5-HT₃ receptors engages spinal rapamycin-sensitive pathways in the rat, *Neurosci. Lett.* 484 (2010) 108–112.