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   2022G008

2. Title

   Roles of Brain Hydrogen Sulfide in Brain Nicotinic Receptor-Induced Suppression of the Micturition Reflex

3. Period

   2022-2024

4. Summary

We performed pharmacological experiments to elucidate mechanisms for brain α7 nicotinic acetylcholine receptor (nAChR)-mediated suppression of the rat micturition reflex, focusing on brain gasotransmitters, hydrogen sulfide (H_2S), nitric oxide (NO) and carbon monoxide (CO). We obtained the following results:

(1) Intracerebroventricular (icv) administration of PHA568487 (PHA, α7 nAChR agonist) at a lower dose (0.3 nmol/rat) had no effect on intercontraction interval (ICI, an indicator of urinary frequency), while under pretreatment with GYY4137 (H2S donor, 3 nmol/rat, icv), PHA (0.3 nmol/rat, icv) prolonged ICI. PHA at a higher dose (1 nmol/rat, icv) induced ICI prolongation, and the PHA-induced prolongation was suppressed by pretreatment with AOAA (H_2S synthase inhibitor, 10 μg/rat, icv).

(2) SNAP (NO donor, 30 nmol/rat, icv) shortened ICI, while L-NAME [NO synthase (NOS) inhibitor, 100 nmol/rat, icv] or B-NI [neuronal NOS (nNOS) inhibitor, 100 nmol/rat, icv] prolonged ICI.

(3) PHA (1 nmol/rat, icv)-induced ICI prolongation was suppressed by pretreatment with SNAP (10 nmol/rat, icv). Under pretreatment with L-NAME (30 nmol/rat, icv), PHA at a lower dose (0.3 nmol/rat, icv) prolonged ICI.

(4) Under pretreatment with CORM (CO donor, 1 nmol/rat, icv), PHA at a lower dose (0.3 nmol/rat, icv) prolonged ICI. PHA (1 nmol/rat, icv)-induced ICI prolongation was suppressed by pretreatment with ZnPP (CO synthase inhibitor, 1 or 10 nmol/rat, icv).

These results demonstrate that (1) brain H_2S and CO are involved in suppression of the micturition reflex caused by activation of brain α7 nAChRs, and (2) brain NO produced by nNOS plays an inhibitory role in the suppression.