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2. Title

Roles of Brain Nicotinic Receptors in Stress-induced Frequent Urination

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4. Summary

We performed pharmacological experiments to elucidate mechanisms for brain nicotinic acetylcholine receptor (nAChR)-mediated suppression of the rat micturition reflex, focusing on the sympatho-adrenomedullary (SA) outflow, brain nAChR subtypes and GABA receptors. We obtained following results:

(1) Intracerebroventricularly (icv) administered (±)-epibatidine (EP), a nAChR agonist, elevated plasma noradrenaline (NA) and adrenaline (Ad) and prolonged intercontraction intervals (ICI, an indicator of urinary frequency), and these EP-induced changes were suppressed by icv pretreated mecamylamine, a nAChR antagonist. On the other hand, intravenous administration of EP showed no effect on ICI.

(2) Acute bilateral adrenalectomy (ADX) abolished the EP-induced elevation of plasma NA and Ad, while the EP-induced ICI prolongation was not influenced by ADX.

(3) The EP-induced ICI prolongation was suppressed by methyllycaconitine (an α7 nAChR antagonist), SR95531 (a $GABA_A$ receptor antagonist) and SCH50911 (a $GABA_B$ receptor antagonist), but not by dihydro-β-erythroidine (an α4β2 nAChR antagonist).

(4) Icv administered PHA568487, an α7 nAChR agonist, prolonged ICI, similar to EP.

Taken together, stimulation of brain α7 nAChRs suppressed the rat micturition reflex through brain $GABA_A$ and $GABA_B$ receptors, independently of the SA outflow modulation. In the future, we should clarify brain α7 nAChR-mediated effects on stress-induced frequent urination in water avoidance stress-exposed rat models.