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Higashi Y, Shimizu T, Yamamoto M, Tanaka K, Yawata T, Shimizu S, Zou S, Ueba T, Yuri K, Saito M. Stimulation of brain nicotinic acetylcholine receptors activates adrenomedullary outflow via brain inducible Nitric oxide synthase-mediated S-nitrosylation. Br J Pharmacol. 2018 Jul 14. doi: 10.1111/bph.14445. [Epub ahead of print] PubMed PMID: 30007012

Higashi et al., have demonstrated that icv administered (±)-epibatidine, a nicotinic acetylcholine receptor (nAChR) agonist, induced secretion of noradrenaline and adrenaline (catecholamines) from the rat adrenal gland medulla with dihydro-β-erythroidine (an α4β2 nAChR antagonist)-sensitive brain mechanisms.

They examined central mechanisms for the (±)-epibatidine-induced responses, focusing on brain nitric oxide synthases (NOSs) and NO-mediated mechanisms, soluble guanylate cyclase and protein S-nitrosylation, in urethane-anaesthetized (1.0 g•kg-1 , ip) male Wistar rats.

EXPERIMENTAL APPROACH: (±)-Epibatidine was icv treated after icv pretreatment with each inhibitor described below. Then, plasma catecholamines were measured electrochemically after HPLC. Immunoreactivity of S-nitrosylated cysteine (SNO-Cys) in α4 nAChR subunit (α4)-positive spinally projecting neurones in the rat hypothalamic paraventricular nucleus (PVN, a regulatory centre of adrenomedullary outflow) after icv (±)-epibatidine administration was also investigated.

KEY RESULTS: (±)-Epibatidine-induced elevation of plasma catecholamines was significantly attenuated by L-NAME (non-selective NOS inhibitor), carboxy-PTIO (NO scavenger), BYK191023 (selective inducible NOS [iNOS] inhibitor) and dithiothreitol (thiol-reducing reagent), but not by 3-bromo-7-nitroindazole (selective neuronal NOS inhibitor) or ODQ (soluble guanylate cyclase inhibitor). (±)-Epibatidine increased the number of spinally projecting PVN neurones with α4- and SNO-Cys-immunoreactivities and this increment was reduced by BYK191023.

CONCLUSIONS AND IMPLICATIONS: Stimulation of brain nAChRs can induce elevation of plasma catecholamines through brain iNOS-derived NO-mediated protein S-nitrosylation in rats. Therefore, brain nAChRs (at least α4β2 subtype) and NO might be useful targets for alleviation of catecholamines overflow induced by smoking. [1)].

1)

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