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INFLUENCE OF 3'-O-METHYL-N-OLEOYL-DOPAMINE ON THE HYPOXIC VENTILATORY RESPONSE IN THE RAT

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3'-O-methyl-N-oleoyl-dopamine (O-Me-OLDA) is the catechol-O-methyltransferase (COMT)-catalyzed methylation product of N-oleoyl-dopamine. The latter is a novel ?lipidized? dopamine compound modulating respiration and interacting with the vanilloid (TRPV1) receptors. The present study seeks to determine whether O-Me-OLDA would exercise an influence on the hypoxic ventilatory response and what receptor pathways would stand behind it. The study was performed in 21 conscious Wistar rats divided into three groups. In the first group we administrated O-Me-OLDA in a single dose of 40 mg/kg. In the two other groups we administrated O-Me-OLDA on the background of either dopamine or vanilloid receptor blockade. We used 5'-iodoresiniferatoxin as a vanilloid antagonist and domperidone as a peripheral D_2 dopamine receptors antagonist. The ventilatory responses to two levels of acute 3-min hypoxia (12 and 8% O_2 in N_2) and hypercapnia (5 and 10% CO_2 in O_2) were investigated in each group, 40 min after administration of O-Me-OLDA. We found that O-Me-OLDA alone decreased the peak hypoxic ventilation by 276 ?66(SE) and 265 ?46 ml/min/kg at 12 and 8% hypoxia, respectively ($P<0.001$). The decreases in the hypoxic responses by O-Me-OLDA became inappreciable after prior D_2 receptor blockade; by 50 ?136 and 96 ?98 ml/min/kg, respectively. In contrast, these decreases were accentuated after prior TRPV1 receptor blockade; by 507 ?55 and 605 ?113 ml/min/kg, respectively. The hypercapnic ventilatory responses remained unaffected irrespective of the condition. In conclusion, the study revealed a dual contrasting action of O-Me-OLDA on the hypoxic ventilatory response: inhibition, being likely mediated by a peripheral carotid body DA pathway, and stimulation, mediated by the TRPV1 receptors. The corollary is that the TRPV1 receptors may be at play in shaping the hypoxic ventilatory response, a hitherto unknown phenomenon.