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THE INFLUENCE OF N-OLEOYL-DOPAMINE ON THE RESPIRATORY RESPONSE TO HYPOXIA IN RATS

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N-oleoyl-dopamine (OLDA) is a fatty acid derivative of dopamine, a key neurotransmitter involved with the hypoxic respiratory response. The aim of our study was to investigate whether N-oleoyl-dopamine would exercise an influence on the respiratory hypoxic response. If that were the case, a second objective would be to investigate whether central or peripheral dopamine pathways were involved in this action. The study was performed on male Wistar rats. The animals were anesthetized, vagotomized, paralyzed, and ventilated. Changes in respiration were evaluated from the product of amplitude and frequency components of the phrenic neurogram. Minute respiratory output was expressed a percent change of the baseline level preceding each test. The experimental protocol consisted of acute responses to two levels of the hypoxic stimulus: 11% O_2 and 14% O_2 in N_2. After taking the control responses, either haloperidol (HAL), a general dopamine receptor antagonist, 0.5 mg/100 g, iv, or domperidone (DOM) – a peripheral dopamine receptor antagonist, 0.3 mg/100 g, ip, was administered, and the hypoxic tests were repeated. After a 20-min interval, OLDA (2 mg/100 g, ip,) was given. The last step was the repetition of the hypoxic responses after another 20-min interval from OLDA injection. In the control group, the administration of the antagonists was omitted. In this group OLDA alone decreased the maximum respiratory hypoxic responses from 147.8 ±10.2(SE)% to 124.1 ±6.8% and from 163.1 ±10.4% to 140.7 ±10.6% of the baseline levels for 14% and 11% hypoxia, respectively. The decrease might be related to the peripheral, carotid body-mediated dopamine-like action. In the antagonist groups, either HAL or DOM also decreased the maximum responses by about 13-17% and 22-30% of the baseline levels for 14% and 11% hypoxia, respectively. OLDA administered after HAL did not appreciably change the maximum responses from the HAL baseline. However, OLDA administered after DOM significantly increased the maximum response to 14% hypoxia, although it did not change that to 11% hypoxia. We conclude that OLDA alone decreases the hypoxic respiratory response but does not change the hypoxic sensitivity. Since the action of OLDA is blocked by HAL, this action may be mediated by dopamine pathways. The persisting increase in the respiratory response to the stronger hypoxia due to OLDA, given after DOM, may have to do with the central stimulatory effect of dopamine. OLDA would then interact with respiration at both central and peripheral levels.

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