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INFLUENCE OF INHIBITION OF PERIPHERAL CATECHOLAMINES ON THE RESPIRATORY RESPONSE TO HYPOXIA IN THE CONSCIOUS RAT

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Monoamino oxidase (MAO) and catechol-O-methyltransferase (COMT) are involved in the inactivation of the catecholamine neurotransmitters (e.g., dopamine). Their specific inhibitors are of increasing research interest, as potential therapy for neurodegenerative brain disorders, like Parkinson?s disease. Our study seeks to determine whether blockade of catecholamine metabolism at the peripheral level, plausibly resulting in an augmentation of the endogenous catecholamine content, could influence the respiratory response to hypoxia which is generated by the peripheral sensory organ of the carotid body. We performed the experiments in 28 conscious Wistar rats (10-11 weeks old). Minute lung ventilation and its responses to 8% and 12% hypoxic stimuli were measured in a BUXCO whole body plethysmographic chamber. After the control recordings had been taken, Debrisoquine, a peripherally acting MAO-A inhibitor (40 mg/kg), or Entacapone, a peripherally acting COMT inhibitor (30 mg/kg), or a combination thereof were injected i.p. and the responses to both stimuli were reevaluated after 30 and 60 min. Debrisoquine stimulated hypoxic ventilation at 30 min; the peak hypoxic ventilation amounted to 1518 ?82(SE) and 1300 ?78 to ml/min/kg before and to 2326 ?302 and 1754 ?309 ml/min/kg after Debrisoquine in response to 8 and 12% hypoxia, respectively. The effect waned at 60 min. Entacapone, on the other hand, failed to influence the responses to hypoxia significantly when injected alone. The effect of Entacapone combined with Debrisoquine corresponded to that of Debrisoquine alone. The increase of hypoxic hyperventilation after MAO-A inhibition suggests that this enzyme predominates in the catecholamine-related mechanisms of the stimulatory ventilatory response to hypoxia in the carotid body and that the dopamine metabolism pathway via COMT is in the carotid body of minor importance.