IMPAIRMENT OF CHEMICAL CONTROL OF BREATHING IN A RESERPINE MODEL OF PARKINSONISM IN THE RAT

Monika Bialkowska[1], Dominika Zajac[1], Pawel Boguszewski[2], Mieczyslaw Pokorski[1]

[1] Department of Respiratory Research, Medical Research Center, Polish Academy of Sciences, Warsaw, Poland

[2] Laboratory of Limbic System, Department of Neurophysiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences

Dopamine (DA) is a well recognized regulator of respiration. The prevailing consensus is that DA is stimulatory for ventilation at the central level and inhibitory peripherally at the carotid body level acting through D2 receptors. The lack of brain DA might impair respiration in Parkinson’s disease (PD). However, studies on respiration in PD are scanty and the results are contentious. Even less is known about the hypoxic ventilatory response (HVR) mediated by the carotid body, which imposes a substantial hyperventilatory strain on the respiratory system. In this study we attempted to differentiate central from peripheral DA role in PD ventilatory changes. We presumed that the lack of carotid body DA could act to uphold the HVR through disfacilitation of DA-mediated inhibition of ventilation. The study was conducted in reserpine plus alpha-methyl-p-tyrosine induced parkinsonism in conscious rats. PD symptoms were confirmed by behavioral tests. Ventilation and its responses to acute hypoxia (8% O2) were investigated in a whole body plethysmograph. We found that the HVR was significantly dampened compared with that in the healthy group. This result ran against our initial presumption and pointed to the plausible predominance of lack of the central DA stimulatory ingredient in the ventilatory impediment of PD. To get insight into the possible role of carotid body DA we then injected domperidone (1 mg/kg, i.p.), a peripheral antagonist of D2 receptors and repeated the HVR. Domperidone caused some rebound of the HVR impairment, which was not significant and much less than domperidone-mediated increase in the HVR present in healthy condition. A minor effect on the impaired HVR of peripheral D2 receptor antagonism makes disfacilitation of DA-mediated ventilatory inhibition at the carotid body level an unlikely occurrence in PD. The study discounts the role of carotid body DA changes in the hypoxic chemoreflex impairment of PD.