INFLUENCE OF TRPV1 (VANILLOID) BLOCKADE ON THE RESPIRATORY RESPONSE TO HYPOXIA AFTER N-OLEOYL-DOPAMINE IN ANESTHETIZED RATS

Dominika Zajac[1], Piotr Roszkowski[2], Zbigniew Czarnocki[2], and Mieczyslaw Pokorski[1]

[1]Department of Respiratory Research, Medical Research Center, Polish Academy of Sciences, Warsaw, Poland;
[2]Division of Organic Chemistry, Faculty of Chemistry, Warsaw University, Warsaw, Poland; dominikazajac@wp.pl

TRPV1 (vanilloid) receptors are ion channels involved in many physiopathogical pathways, e.g., in the sensation and transmission of pain and temperature stimuli. Being ion channels present in airways and in the brain, these receptors could possibly take part in shaping the respiratory response to hypoxia, especially in the context of the interaction of vanilloids with carotid body function, the sensory organ responsible for the generation of such a response. It is known that N-oleoyl-dopamine (OLDA), a novel lipid derivative of dopamine with vanilloid-like activity depresses the ventilatory response to hypoxia. In the present study we investigated the hypothesis that the ventilatory effects of OLDA could have to do with the TRPV1 receptors. The experiments were performed in 7 anesthetized, vagotomized, paralyzed, and ventilated rats. Changes in respiration were evaluated from the product of the amplitude and frequency components of phrenic neurogram. Minute respiratory output was expressed as a percent change from the baseline level preceding each test. The experimental protocol consisted of taking the acute responses to two levels of the hypoxic stimulus: 11% O2 and 14% O2 in N2. After taking the control responses, 5'iodoresiniferatoxin (5'IRTX, 0.4 mg/kg, i.p.), a total TRPV1 antagonist, was given and the hypoxic tests were repeated. Then, OLDA (20 mg/kg, i.p.) was administered and both hypoxic tests were repeated. We found that TRPV1 receptor blockade, in itself, did not significantly change the response of neural respiratory output to hypoxia. The peak minute respiratory output increases were by 37.1 +/-4.9(SE)% and 102.8 +/-32.1% before and by 38.3 +/-17.5% and 101.2 +/-48.4% after the blockade for the 14% and 11% hypoxia, respectively. Nor were there any appreciable changes in the interplay of the frequency and volume components making up minute respiratory neural output. Moreover, 5'IRTX did not influence the latter depressant phase of the respiratory response to hypoxia either, although the interpretation of the results is hindered by a substantial scatter of individual results. Furthermore, the lowering of the hypoxic respiratory responses by OLDA was sustained when it was given after TRPV1 receptor blockade; the decreases in peak minute neural phrenic response, 40 sec from hypoxia induction, were from 138.3 +/-17.5 to 115.8 +/-21.6% and from 201.2 +/-48.4 to 111.6 +/-12.7% of the baseline level for 14% and 11% hypoxia, respectively. In conclusion, the lack of respiratory effects of TRPV1 receptors blockade with 5'-iodoresinifaratoxin speaks against their active role in chemical regulation of respiration, at least in the experimental animal model used, that is in anesthetized rats being in the neural open-loop condition. Therefore, the inhibitory action of OLDA on the ventilatory response to hypoxia is mediated rather by other than the TRPV1 pathways.