HIGHLIGHTED TOPIC | Oxygen Sensing in Health and Disease

Understanding the critical role of oxygen sensing in the physiological states of health and disease is important to our understanding of disease processes. This issue of the Journal concludes the Highlighted Topics series on “Oxygen Sensing in Health and Disease” and includes two articles that warrant comment, as they represent significant contributions to our general understanding of the mechanisms underlying oxygen sensing.

In the first featured article, “Peripheral chemoreflex responsiveness is increased at elevated levels of carbon dioxide after episodic hypoxia in awake humans,” Dr. J. Mateika and colleagues (2) discuss the influence of episodic hypoxia on ventilatory response. After exposing awake humans to episodic hypoxia, these investigators evaluated the acute ventilatory response to hypoxia in the presence of progressively increasing levels of carbon dioxide. Their study showed that the ventilatory response to hypercapnia/hypoxia, but not hypocapnia/hypoxia, was increased after exposure to episodic hypoxia. This response was evident even though elevated ventilation levels (i.e., long-term facilitation) were not observed immediately after exposure to episodic hypoxia. These findings may have important implications for the control of breathing in individuals who suffer from sleep apnea. Disproportionate increases in the ventilatory response to hypercapnia/hypoxia after exposure to episodic hypoxia could subsequently drive carbon dioxide levels below the apneic threshold. Consequently, a reduction in central respiratory drive to chest wall and upper airway muscles might occur, and activation of this phenomenon might thus promote apnea during sleep.

The second featured article, “Facilitation of dopamine and acetylcholine release by intermittent hypoxia in PC12 cells: involvement of calcium and reactive oxygen species” by Dr. D.-K. Kim and colleagues (1), reports, for the first time, the effect of intermittent hypoxia on transmitter release during hypoxia and examines the underlying cellular mechanisms that are activated and lead to altered transmitter release. These investigators simultaneously monitored the release of dopamine and acetylcholine from both naive and intermittent hypoxia-conditioned PC12 cells by using two dedicated and highly sensitive HPLC systems combined with an electrochemical detection method. From these measurements, the authors made an intriguing observation, wherein hypoxia selectively facilitates the release of dopamine, but not acetylcholine, in naive cells. By contrast, hypoxia increased the release of both dopamine and acetylcholine in intermittent hypoxia-conditioned cells. Notably, the mechanisms that are activated by intermittent hypoxia and coupled to intermittent hypoxia-evoked transmitter release seem to be different from those activated during acute hypoxia. In naive cells, the entry of extracellular calcium appears to be critical for hypoxia-evoked dopamine release. On the contrary, intermittent hypoxia-induced transmitter release during hypoxia depends on the mobilization of calcium from intracellular stores through activation of inositol 1,4,5-trisphosphate receptors, as well as generation of reactive oxygen species.

REFERENCES

1. Kim DK, Natarajan N, Prabhakar NR, and Kumar GK. Facilitation of dopamine and acetylcholine release by intermittent hypoxia in PC12 cells: involvement of calcium and reactive oxygen species. J Appl Physiol 96: 1206–1215, 2004.

2. Mateika JH, Mendello C, Obeid D, and Badr MS. Peripheral chemoreflex responsiveness is increased at elevated levels of carbon dioxide after episodic hypoxia in awake humans. J Appl Physiol 96: 1197–1203, 2004.

Gary C. Sieck
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