

# Regulation of diaphragmatic nitric oxide synthase expression during hypobaric hypoxia.

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## Abstract

Nitric oxide (NO) is normally synthesized inside skeletal muscle fibers by both endothelial (eNOS) and neuronal (nNOS) nitric oxide synthases. In this study, we evaluated the influence of hypobaric hypoxia on the expression of NOS isoforms, argininosuccinate synthetase (AS), argininosuccinate lyase (AL), and manganese superoxide dismutase (Mn SOD) in the ventilatory muscles. Rats were exposed to hypobaric hypoxia (approximately 95 mmHg) from birth for 60 days or 9-11 mo. Age-matched control groups of rats also were examined. Sixty days of hypoxia elicited approximately two- and ninefold increases in diaphragmatic eNOS and nNOS protein expression (evaluated by immunoblotting), respectively, and about a 50% rise in diaphragmatic NOS activity. In contrast, NOS activity and the expression of these proteins declined significantly in response to 9 mo of hypoxia. Hypoxia elicited no significant alterations in AS, AL and Mn SOD protein expression. Moreover, the inducible NOS (iNOS) was not detected in normoxic and hypoxic diaphragmatic samples. We conclude that diaphragmatic NOS expression and activity undergo significant adaptations to hypobaric hypoxia and that iNOS does not participate in this response.