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**Oxygen insufficiency during hypoxic hypoxia in rat brain cortex.**

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To relate cerebral oxygen sufficiency and insufficiency with arterial oxygen tension, reduction/oxidation responses of the initial and terminal members of the mitochondrial respiratory chain (NADH and cytochrome c oxidase) were recorded in situ by optical techniques when increased cerebral energy use was provoked by direct electrical stimulation. Small decreases in  $paO_2$ , produced by forced ventilation of hypoxic gas mixtures, resulted in decreased amplitude of the characteristic negative shift in extracellular potential which accompanies such stimulation and smaller oxidative response of NADH and cytochrome oxidase. When  $paO_2$  fell below 40-50 Torr, stimulation produced reductive rather than oxidative shifts of the mitochondrial respiratory chain components. The data suggest that when arterial oxygen tension is slightly decreased, compensating mechanisms allow brain function to continue with minimal changes in cortical metabolites and high energy phosphate compounds. When arterial oxygen falls below 40-50 Torr, however, compensation can no longer prevent tissue hypoxia during times of increased energy demand. Thus, hypoxemia is not necessarily synonymous with oxygen insufficiency, but oxygen sufficiency must be defined with due regard to the degree of energy demand.

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