DYNAMIC HYPOXIC HYPOXEMIA IN BRAIN TISSUE: EXPERIMENTAL AND
THEORETICAL METHODOLOGIES

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An experimental system was assembled to study feline cerebral cortex cellular and extracellular pO\textsubscript{2} response to rapid changes in carotid artery oxygen levels. The system has been described in prior articles in this series and elsewhere (Bogue and Dorson, 1973; Dorson and Bogue, 1973; Dorson and Bogue, 1976; Bogue, 1974). Changes in carotid artery oxygen level could be accomplished either by varying the ventilatory gas composition or by a carotid-jugular computer controlled exchange method. The latter technique involved cannulation of both internal carotid arteries and jugular veins. All other perfusion routes were suppressed by compression. Relatively open flow was allowed in both directions with exchange between venous and arterial blood on an equal volume flow basis. This system resulted in the most rapid possible input change while maintaining close to normal physiological function. Many different types of changes were investigated, and this report will concentrate on oscillatory inputs caused by both the ventilation gas and blood exchange methods. No difference in response was noted up to the upper frequency limit of the ventilation method of 0.1 Hz while the exchange method was capable of 1.0 Hz oscillations.

Microelectrodes were used to measure arterial pO\textsubscript{2}, intracellular pO\textsubscript{2} (and action potentials), and venous pO\textsubscript{2}. Other continuous measurements included EKG, temperature, arterial blood pressure, and total carotid brain blood flow. Serial arterial and venous samples were drawn for pH, pCO\textsubscript{2}, pO\textsubscript{2} (calibration check), Hb, hematocrit, and O\textsubscript{2} content. The serial measurements were used to calculate the total brain metabolic O\textsubscript{2} consumption which, on a per 100 gm basis, determined the physiological condition of the preparation at that time.
The theoretical model contained three capillary blood compartments (in series) with mass transfer to two parallel interstitial fluid compartments. Two cellular compartments were then placed in series with the extracellular compartments. To simulate the experimental arrangement both a time delay and mixing compartment separated the appropriate capillary compartment from either the arterial or venous measurement site. A four step kinetic metabolic model was included into each of the two intracellular compartments. Theoretical calculations could be compared to the experimental data in several ways (see Dorson and Bogue, 1973; Dorson and Bogue, 1976 for more details). For any arterial oxygen waveform a direct comparison of predicted and experimental tissue or venous pO₂ with time was possible. For oscillatory waveforms the entire test period could be signal averaged to produce tissue (or venous) to arterial pO₂ amplitude ratios for comparison purposes. The third method was to produce auto- and cross-correlations between any two recorded or predicted signals. This technique again averaged the response over the entire test period and eliminated any unrelated noise.

The problem with these experiments, in addition to the instrumental complexity, is that total brain perfusion values are combined with single cell measurements. The brain is both inhomogeneous and subject to selective recruitment in response to changing perfusion conditions. The tissue probe location variable could be easily accounted for through the pO₂ absolute value with the transfer coefficients. This straightforward approach is also consistent with multiple probe observations in the brain cortex during extended hypoxia induced by ventilatory gas composition changes (Leniger-Follert et al, 1976). However, significant variations in local blood flow rate changes were also noted in the referenced work.

The lack of exact correspondence between local and total brain blood flow is an obstacle to the application of theoretical predictions herein. For temporal comparisons this situation could be partially overcome by obtaining a large number of similar experiments and using a global average response. A less satisfactory approach for oscillatory waveforms would be to assume that the average local tissue response over an extended test period would be directly related to the total brain input and response changes.

RESULTS

The major goal of the exchange system was to achieve extremely rapid carotid artery pO₂ waveforms. This is also a significant difference between these results and prior investigations. Exchange system step changes were analogous to a square wave arterial pO₂ input while ventilation gas changes were analogous to a slow ramp function.

The most important determinant of the type of response was the