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ANNEXE 2

Journal of Cerebral Blood Flow and Metabolism
Vol. 1, Suppl. 1, © 1981 Raven Press, New York

I-4 Measurement of Regional Oxygen Consumption by Positron Emission Tomography

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The quantitative measurement of regional cerebral metabolic rate for O_2 ($rCMRO_2$) by PET has been difficult, because O_2 is rapidly converted to H_2O by brain and discharged. Attempts to circumvent this problem by utilizing the dynamic equilibrium distribution of the continuously inhaled gases $O^{15}O$ and $C^{15}OO$ have met with some success (1), but this approach is time consuming and encounters a number of computational uncertainties. A rapid, efficient, multislice PET deivce has allowed us to adopt an adaptation of our general model for the measurement of metabolic rates with PET (2). Elements of this model and, hence, uncertainties about the behavior of unmetabolized tracer in tissue have been eliminated because (1) O_2 enters tissue by simple diffusion and (2) tissue contains negligible free O_2. Our approach is embodied in the following equation:

$$CMRO_2 = \frac{q(t) - C_b V_b a_b(t) + \gamma C_b V_b [\int_o^t a_b(u)du - a_b(t) * e^{-t/\tau}]}{\int_o^t a_b(u)du}$$

In this equation, q represents the local molar mass of radio-oxygen within a spatial resolution element of the detector; the a's represent radio-oxygen specific activities; and the subscript b denotes blood. C_b is the oxygen concentration in arterial blood and V_b is the local blood volume (measured independently with ^{15}O-carbon monoxide) in a detector resolution element. This equation contains a new term in the numerator (2) allowing us to describe the behavior of metabolic $H_2{}^{15}O$. In this new term the parameter τ is equivalent to (blood flow)$^{-1}$. The parameter γ represents a composite of parameters characterizing the tissue solubility, permeability and distribution of oxygen and water. Approximate values for the term τ can be obtained from measurements of local blood flow as detailed elsewhere in this volume (3). Because $H_2{}^{15}O$ is used forsuch measurements τ is overestimated at higher flows because water does not move freely between blood and brain (4). However, the whole term in which τ is contained is relatively insensitive to such errors, thus an approximate estimate is sufficient. γ has a value between 0.01 and 0.05 sec^{-1}. Although our data is insufficient to estimate this parameter directly in each case, average values suffice because of the relative insensitivity of the measurement of local $CMRO_2$ to this parameter as well as τ.

Operationally, our measurement requires a single breath of $O^{15}O$ and 40 seconds of data collection. In a variety of studies (computer simulations, animal experiments), we have satisfactorily tested the validity and realm of applicability of this method. Studies in human subjects indicate that it is a highly satisfactory method for the rapid (<1 min) and quantitative measurement of $rCMRO_2$ with PET (Fig 1).

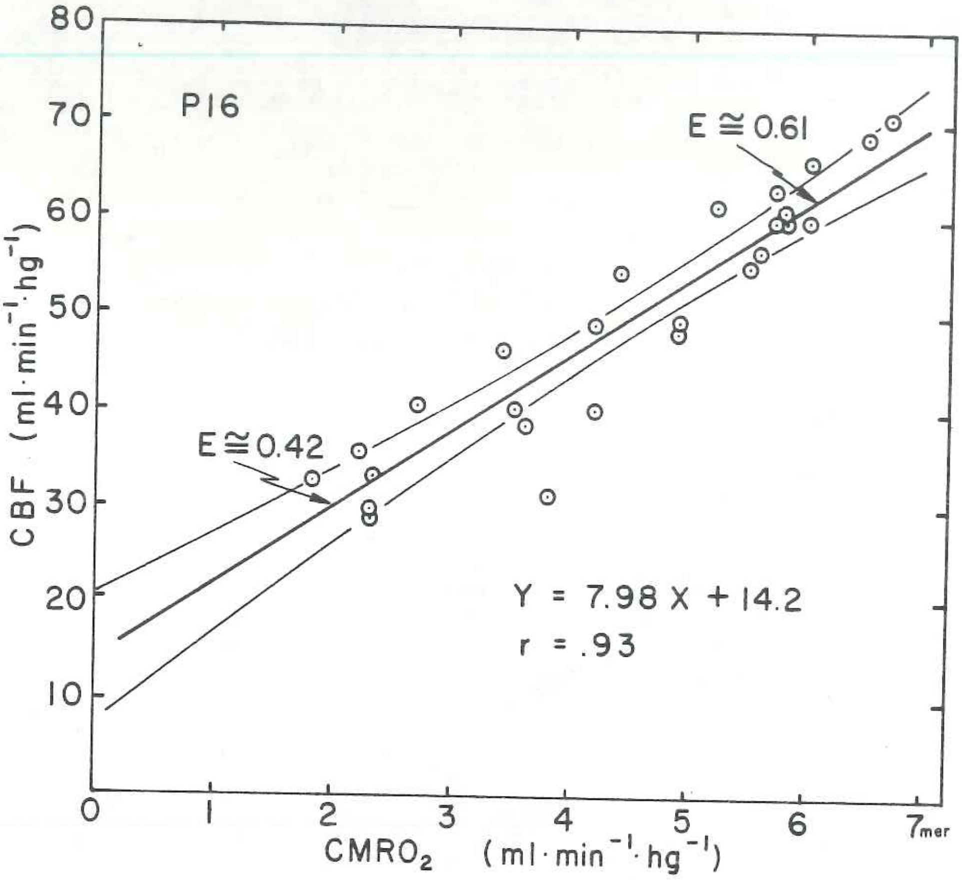

Figure 1: Regional measurements of local cerebral metabolic rate for oxygen ($CMRO_2$) and local cerebral blood flow in a normal adult using positron emission tomography (PET). Regions were selected randomly to represent areas of high and low $CMRO_2$ and CBF. CBF was measured locally by a new technique described elsewhere in this volume (3) and $CMRO_2$ by the method described in this paper. The local extraction of O_2 is E in the figure. It should be noted that E increases with the local $CMRO_2$ and CBF suggesting that flow is not perfectly matched with the local oxygen demands even in the normal brain.

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