roid target neurons. Steroid-binding neurons would be most likely in those species, like the toadfish, that produce a seasonal, sexually dimorphic mating call with functions similar to those of bird song (*4*, *14*).

Except for the sexually dimorphic nuclei of rats involved in female lordosis (*21*), neurons innervating perineal muscles in males (*22*), and the nuclei associated with sound production in various vertebrates (*3*), the behavioral functions of steroid target neurons are largely unknown. Steroids are usually considered to have two types of actions on the central nervous system (*21*), an organizational effect (that is, sexual differentiation of the brain and determination of the structure and complexity of neural circuits) and an activating or inhibiting effect on preexisting neural circuits (by affecting neuronal electrical activity and synaptic transmission). Activation of behavior also parallels the ethologists' notion of the effect of steroids on the fixed action pattern. The two types of actions do not, however, include the possibility that steroids can modulate quantitative aspects of a behavior pattern. For instance, the pitch of the contact call of the Japanese quail varies directly with androgen concentration (*23*), and quantitative seasonal changes in the toadfish boatwhistle are only partially related to temperature (*14*). Identification of two sets of target neurons in the toadfish medulla, at the approximate levels predicted for pattern generators by Demski (*13*), makes control and modulation of call duration and fundamental frequency an attractive hypothesis for the function of these nuclei. It also extends the correlation between sound production and neuronal steroid uptake to a member of the largest vertebrate class, the fishes.

MICHAEL L. FINE
Department of Biology, Virginia Commonwealth University, Richmond 23284
DONALD A. KEEFER
Department of Anatomy, University of Virginia School of Medicine, Charlottesville 22908
GEORGE R. LEICHNETZ
Department of Anatomy, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298

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In vivo Mapping of Local Cerebral Blood Flow by Xenon-Enhanced Computed Tomography

Abstract. *A noninvasive technique has been developed to measure and display local cerebral blood flow (LCBF) in vivo. In this procedure, nonradioactive xenon gas is inhaled and the temporal changes in radiographic enhancement produced by the inhalation are measured by sequential computerized tomography. The time-dependent xenon concentrations in various anatomical units in the brain are used to derive both the local partition coefficient and the LCBF. Functional mapping of blood flow with excellent anatomical specificity has been obtained in the baboon brain. The response of LCBF to stimuli such as changes in carbon dioxide concentrations as well as the variability in LCBF in normal and diseased tissue can be easily demonstrated. This method is applicable to the study of human physiology and pathologic blood flow alterations.*

The importance of techniques that can be used to measure cerebral blood flow as an index of cerebral function has long been recognized. A number of techniques have been developed in an attempt to find an in vivo methodology to map local or regional cerebral metabolic rate or cerebral blood flow, or both, for normal or abnormal brain function (*1*, *2*). In most methods currently in use, one externally monitors the transit or clearance of inhaled or injected radiotracers (*2–4*). Although these techniques have proved useful, they generally yield only gross estimates of cerebral function within relatively large tissue volumes. Recent advancements in both single-photon and positron-annihilation emission computed tomography permit improved anatomical resolution (*5*, *6*). These techniques still suffer from inherent limitations of spatial resolution and require specialized imaging devices (*6*, *7*). The introduction of rapid, sequential transmission computed tomography (CT) provided a method of monitoring changing tracer concentrations over time with improved anatomical specificity (*8*). Although iodinated contrast media have been used to demonstrate qualitative flow patterns, methods developed to make quantitative measurements of local cerebral blood flow have had only limited success. In addition, clinically available contrast media do not cross the blood-brain barrier; therefore, tissue perfusion in the brain cannot be evaluated (*9*).

We have been developing techniques over the past several years in which local cerebral blood flow (LCBF) in extremely small tissue volumes in vivo can be de-

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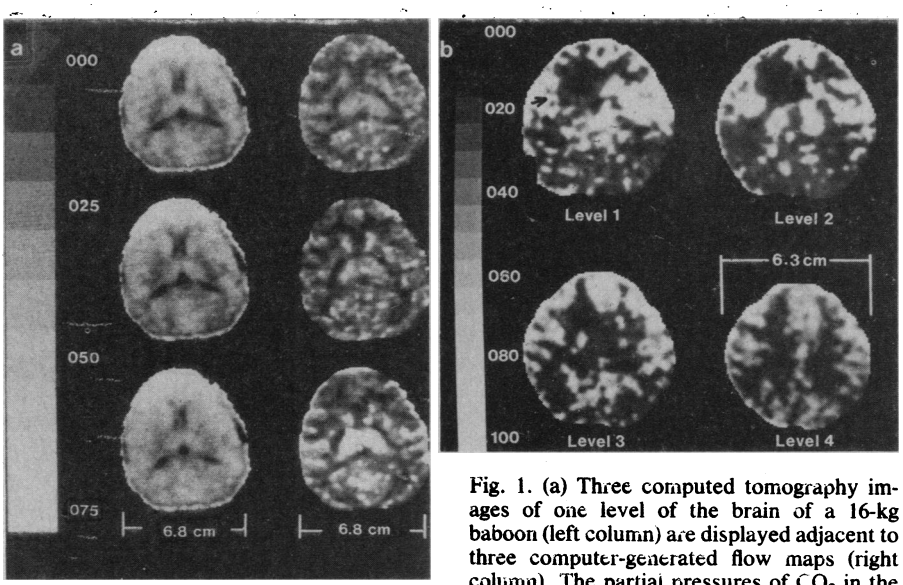

Fig. 1. (a) Three computed tomography images of one level of the brain of a 16-kg baboon (left column) are displayed adjacent to three computer-generated flow maps (right column). The partial pressures of CO_2 in the flow studies were 38, 44, and 55 torr for the upper, middle, and lower images, respectively. Elevated blood flow in various locales, mostly gray matter, with increased CO_2 concentrations are readily observed. The gray scale is given in milliliters per 100 g per minute. (b) Multilevel blood flow maps of four adjacent brain sections (5 mm thick) of a 9.8-kg baboon 19 days after infarction (arrow). Level 4 is above the infarcted area. All four sections were studied during a single inhalation.

rived from measurements of time-dependent concentrations of nonradioactive xenon gas. In these methods one uses sequential CT scanning of one or more brain levels (slices) during the inhalation of xenon-oxygen mixtures to detect the buildup of xenon in tissue. Since xenon is a freely diffusible tracer which readily crosses the blood-brain barrier, its concentration in tissue serves as an indicator of tissue perfusion. Because of its relatively high atomic number (54), xenon yields measurable image enhancement even when it is inhaled in relatively low concentrations. The derivation of LCBF is based on the Fick principle, and the underlying relationship has been described by Kety (*10*); details of the methodology for deriving LCBF estimates from enhanced xenon CT have been described (*11*). In brief, the procedure requires the acquisition of three to five images preceding and during 4 to 6 minutes of xenon-oxygen inhalation. During this period the xenon concentrations in inspired and expired gas are monitored continuously, and end-tidal xenon concentrations are assumed to be proportional to time-dependent xenon concentrations in arterial blood (*4*). These data are then used in conjunction with time-dependent xenon concentrations in tissue to derive partition coefficients (λ) and LCBF by multivariable analysis. A major advantage of this methodology is that both λ and LCBF can be derived simultaneously for each specific tissue of interest.

Recently we have been able to use this technique to generate LCBF maps in lightly anesthetized and awake primates. A "sliding window" filter, used to reduce system noise by smoothing out pixel-to-pixel variations, precedes the derivation of blood flow estimates for each pixel (Fig. 1a). The resultant blood flow maps can be displayed adjacent to the standard morphologic CT images. Both anatomical specificity (resolution, full width at half-maximum $\leq$ 4 mm) and easily observable variations in blood flow within normal and abnormal tissue are achievable (Fig. 1b), as are alterations in blood flow that occur in response to stimuli such as changes in the CO_2 concentrations (Fig. 1a) (*12*).

These techniques are presently being investigated for possible routine clinical use. Although such use is the ultimate goal of these investigative efforts, the additional information concerning normal and diseased animal tissue function is of extreme importance as well. Animal studies may enhance our understanding of the mechanisms of altered function resulting from such conditions as infarction or tumors and may provide the means for monitoring the effects of therapeutic efforts on local or regional tissue function. The anticipated benefits to humans include significantly improved measurement of tissue perfusion in the boundary of a developing brain infarct (evolving stroke) and in brain tissue with relative ischemia (threatened or impending stroke) and the correlation of metabolism and blood flow patterns with anatomical structures (tracts and nuclei) in chronic demyelinating and degenerative central nervous system syndromes. Such information may also prove valuable in the early diagnosis of these conditions.

DAVID GUR
Departments of Radiation Health and *Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania 15261*
WALTER F. GOOD
Department of Radiation Health, University of Pittsburgh
SIDNEY K. WOLFSON, JR.
Department of Neurological Surgery, University of Pittsburgh, and *Laboratory of Surgical Research, Montefiore Hospital, Pittsburgh*
HOWARD YONAS
Department of Neurological Surgery, University of Pittsburgh
LEONARD SHABASON
Departments of Radiation Health and *Radiology, University of Pittsburgh*

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David Gur, Walter F. Good, Sidney K. Wolfson, Jr., Howard Yonas, and Leonard Shabason

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