PET in Cerebrovascular Disease

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KEYWORDS

- Positron emission tomography
- Cerebrovascular disease • Vascular dementia
- Cerebral blood flow • Cerebral metabolism
- Cerebral hemodynamics

Cerebrovascular disease results from a derangement of the normal relationship between the cerebral vasculature and the brain parenchyma. Thus, investigation of the interplay between the cerebral circulation and brain cellular function is fundamental to understanding both the pathophysiology and treatment of stroke. At present, PET is the only technique that provides accurate, quantitative in vivo regional measurements of both cerebral circulation and cellular metabolism in human subjects. PET is therefore well suited for the study of human cerebrovascular disease, but its application to this end is not easy. An on-site cyclotron and radiochemistry facility is necessary due to the short half-lives of the commonly used radionuclides ^{15}O (2 minutes) and ^{11}C (20 minutes). Quantitative physiologic measurements require complex post-processing and multiple arterial blood samples, although for some specific applications simple count-based images can be used.[1,2] Patients with acute stroke may be medically unstable, requiring a nurse or physician in attendance. For these reasons, PET is still a research tool for cerebrovascular disease. PET has provided us with valuable new knowledge and insight into both ischemic and hemorrhagic stroke regarding pathophysiology, therapy, and prognosis but has not entered the mainstream of clinical practice. In the future, the results of the Carotid Occlusion Surgery Study (www.cosstrial.org), an ongoing clinical trial in which PET is being used to determine eligibility, may demonstrate the clinical value of PET for the routine management of cerebrovascular disease.

NORMAL CEREBRAL HEMODYNAMICS AND ENERGY METABOLISM

Energy in the brain is used for the maintenance of membrane potentials, for the biosynthesis and transport of neurotransmitters, and for the biosynthesis and transport of cellular elements. Under normal circumstances the brain relies on a continuous supply of oxygen and glucose from the blood for its functional and structural integrity.[3] Because storage of substrates for energy metabolism in the brain is minimal, it is exquisitely sensitive to even brief disturbances in this supply. Complete interruption of the cerebral circulation in cardiac arrest causes loss of consciousness within 10 seconds.[4]

This work was supported by USPHS grants NS06833, NS35966, NS044885 and NS42167 and the H. Houston Merritt Distinguished Professorship at the University of North Carolina School of Medicine.

NOTE: None of the PET radiopharmaceuticals mentioned in this article is FDA-approved for use in patients with cerebrovascular disease.

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PET Clin 5 (2010) 83–106
doi:10.1016/j.cpet.2009.12.007

Healthy young adults have an average whole brain cerebral blood flow (CBF) of approximately 46 mL $100g^{-1}$ min^{-1}, cerebral metabolic rate of oxygen ($CMRO_2$) of 3.0 mL $100g^{-1}$ min^{-1} (134 μmol $100g^{-1}$ min^{-1}), and cerebral metabolic rate of glucose (CMRglc) of 25 μmol $100g^{-1}$ min^{-1}.[5–8] The $CMRO_2$/CMRglc molar ratio calculated from arterio-jugular venous differences is 5.4 rather than 6.0, as expected for complete oxidation because of the production of a small amount of lactate by glycolysis.[5,7,9] CBF in gray matter (80 mL $100g^{-1}$ min^{-1}) is approximately 4 times higher than in white matter (20 mL $100g^{-1}$ min^{-1}), but differences of this magnitude are not seen with PET due to partial volume effects.[10] Under normal physiologic conditions, regional CBF is closely matched to the resting regional metabolic rate of the tissue.[11,12] As with CBF, $CMRO_2$ and CMRglc are higher in gray than white matter. Because of this relationship between regional flow and metabolism, the fraction of available glucose and oxygen extracted by the brain from the blood is uniform throughout the brain (**Fig. 1**). The oxygen extraction fraction (OEF) is normally 30% to 40%, indicating that oxygen supply is 2 to 3 times greater than oxygen demand. The glucose extraction fraction (GEF) is normally about 10%.[12,13]

Many studies report that CBF declines from the third decade onward.[14–17] The change in metabolic rate for oxygen and glucose with age is less clear, with several studies showing a decrease[14,16,18–20] and others showing no change.[21–23] Studies that have corrected for brain atrophy show lesser or absent changes in CBF, $CMRO_2$, and CMRglc with increasing age.[19,24–26] The authors' own PET data corrected for brain atrophy from 23 normal subjects, age 23 to 71 years, show no significant change in CBF or $CMRO_2$, but a decline in CMRglc of 4% to 5% per decade.

CEREBROVASCULAR CONTROL

Regional CBF is determined by the local cerebral perfusion pressure (CPP) and the local cerebrovascular resistance (CVR).

$$CBF = \frac{CPP}{CVR}$$

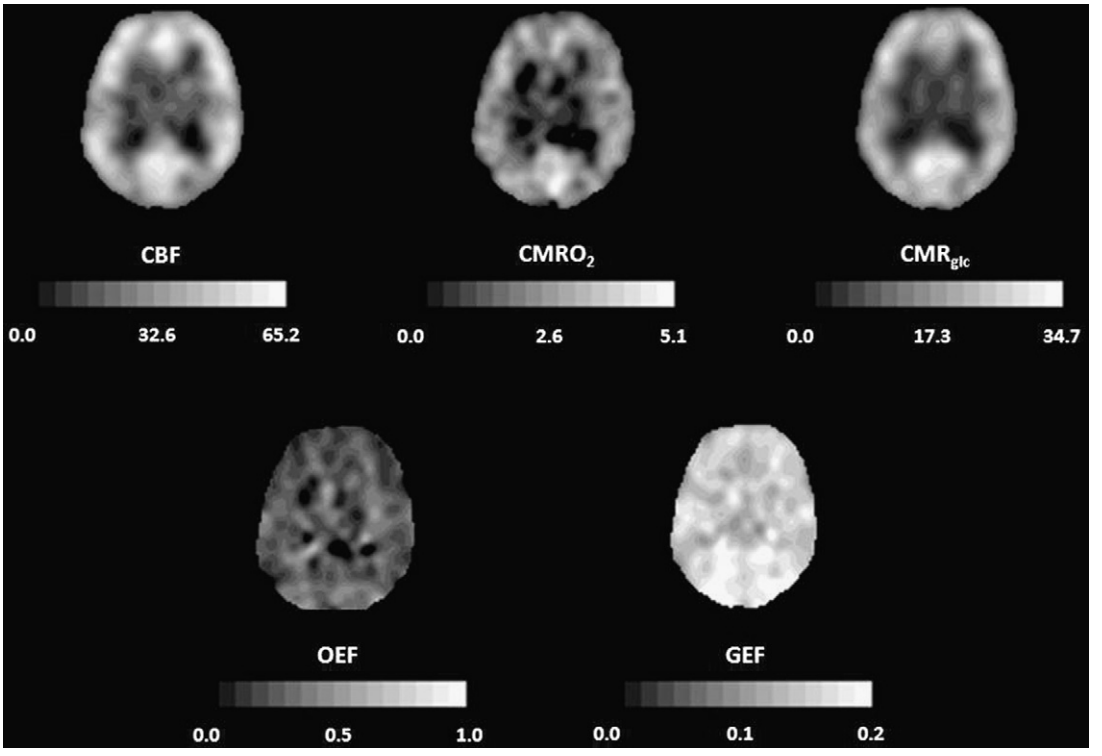

Fig. 1. Normal cerebral blood flow and metabolism. PET scans from a normal 70-year-old woman. Cerebral blood flow (CBF, mL $100g^{-1}$ min^{-1}), cerebral metabolic rate of oxygen ($CMRO_2$, mL $100g^{-1}$ min^{-1}), and cerebral metabolic rate of glucose (CMRglc; μmol $100g^{-1}$ min^{-1}) all show higher values in cortex that in white matter. Oxygen extraction fraction (OEF) and glucose extraction fraction (GEF) are relatively uniform throughout the brain. (*From* Powers WJ, Zazulia AR. The use of positron emission tomography in cerebrovascular disease. Neuroimaging Clin N Am 2003;13:742; with permission.)