Clinical Applications for the Central Nervous System

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The glucose metabolism of the brain can be evaluated using the glucose analog, $^{18}$F-fluorodeoxyglucose (FDG). FDG is transported into the cells by the same mechanism as glucose. FDG is then phosphorylated by a hexokinase into FDG-6-phosphate. As brain tissue does not have a glucose-6-dephosphatase, FDG-6-phosphate cannot progress into further glycolytic pathways, so it accumulates proportional to the glycolytic rate of the cells. The cortex of the brain normally only uses glucose as its substrate; therefore, FDG accumulation is high. Because dedicated PET systems with full rings of bismuth germanate oxide (BGO) detectors provide for soft tissue attenuation and are calibrated with an external source of known activity of $^{68}$germanium, true count rates can be measured over a region of interest. Dynamic scanning after injection of FDG and dynamic arterial blood sampling to obtain both tissue and plasma tracer concentrations over time permit quantification of the actual metabolic rate using kinetic modeling. True quantitative measurements are extremely useful in the investigation of the physiopathological mechanisms of neuropsychiatric diseases and can be performed not only with FDG, but also with a variety of other radiopharmaceuticals labeled with positron emitters. This approach is time-consuming, cumbersome, and more invasive than obtaining a static image after FDG reaches a plateau, usually 45 minutes following intravenous injection. Measurement of the absolute metabolic rate is rarely performed clinically. Semiquantitative evaluation with asymmetry indices or ratios to reference structures of the brain is usually satisfactory for clinical diagnostic purposes. Correction for attenuation can be performed using transmission maps, obtained from external radioactive sources (measured attenuation correction), or using calculated attenuation correction. Correction for attenuation effects can be performed using calculated geometric attenuation for uniform structures that are predictable in shape and content, such as the brain. Calculated attenuation correction can be used very accurately and is patient-independent.

To interpret tomographic cerebral images, it is critical to utilize software capable of reorienting the images along the anterior commissure-posterior commissure (AC-PC) line. The images should be viewed on a monitor in all three projections (axial, coronal, and sagittal), utilizing color scales and gray scale with appropriate intensity settings. If two sets of images must be compared (ictal and interictal, baseline and activation, pre- and post-therapy or intervention), similar orientation, section thickness, and windowing is critical. Comparison with current MRI or CT images is also critical to correlate with structural abnormalities.

Normal Distribution and Variants

Perfusion and glucose metabolic images of the brain have a similar appearance, except in pathologic circumstances when there is decou-
pling of perfusion and metabolism. The adult pattern of uptake is established by age two. The normal perfusion of the gray matter is approximately 70 ml/min/100 g, and that of the white matter is 20 ml/min/100 g. In the newborn, the perfusion and metabolism of basal ganglia, visual cortex, and sensory-motor cortex are similar to that of an adult, but there is relative decreased perfusion to the frontal and parieto-temporal cortices, giving an immature pattern of perfusion and metabolism. This must be recognized to accurately interpret metabolic PET images in children under age two.

The weight of the brain decreases approximately 10% between the ages of 30 and 75, and the cerebral blood flow decreases by 20%, probably because of neuronal loss and replacement by gliosis. On CT and MRI, this is demonstrated by progressive cortical atrophy with age.

In normal individuals, cerebral perfusion and metabolism are both influenced by certain drugs. Sedatives decrease the cerebral blood flow and metabolism. If a patient requires sedation for the scanning period, sedatives should be administered no earlier than 30 minutes after administration of the radiopharmaceutical. It is important to be aware of the medications taken by patients and their effects on the pattern of cerebral perfusion and metabolism.

Cerebral Vascular Disease

The etiologies of a cerebral infarction are multiple: thrombotic, embolic, and hemorrhagic, among others. Functional images are usually abnormal before anatomical images because the physiological dysfunction of an organ precedes the resulting anatomical changes. Positron emitters include $^{15}$oxygen (half-life = 2 minutes), $^{13}$nitrogen (half-life = 10 minutes), $^{11}$carbon (half-life = 20 minutes), and $^{18}$fluorine (half-life = 110 minutes) and require coincidence detection with a PET scanner for imaging. These radioisotopes have the advantage of being innate to the molecular structure of endogenous substrates. PET studies using $^{15}$O-H$_2$O to evaluate perfusion, $^{15}$O-O$_2$ to evaluate oxygen metabolism, and $^{18}$F-FDG to evaluate glucose metabolism have contributed to the understanding of the physiopathology of cerebral infarction. Because of the short half-life of positron emitters, these PET radiopharmaceuticals are not practical for clinical use, except for $^{18}$F-FDG.

Within the first hours to days after a stroke, there is decreased relative perfusion compared to glucose and oxygen metabolism, a phenomenon called “misery perfusion.” Twenty-four hours to one week after infarction, the perfusion usually improves, but the symptoms and crossed cerebellar diaschisis persist. There is decoupling of metabolism and perfusion, a phenomenon called “luxury perfusion,” that may last from one to ten days and is thought to be due to local accumulation of free radicals. The “luxury perfusion” usually resolves one month after the acute event. In addition, there exists a “penumbral zone” surrounding the infarcted area, which is ischemic and demonstrates decreased perfusion but increased oxygen extraction fraction. If perfusion to the “penumbral zone” can be restored in a timely manner, irreversible damage will not occur.

There are regions that show decreased perfusion and metabolism that are distant to the region of infarction. For example, cortical infarcts are usually associated with decreased uptake in the contralateral cerebellar hemisphere (crossed cerebellar diaschisis) due to deafferentation, a phenomenon that occurs when the impulses through the cortico-ponto-cerebellar fibers fail to be transmitted and stimulate the contralateral cerebellar hemisphere. Other areas that can demonstrate decreased perfusion and metabolism are the ipsilateral thalamus and caudate nucleus, probably also related to deafferentiation. Infarction of specific thalamic nuclei results in cortical hypometabolism, while infarction of others do not, due to specific thalamocortical tracts.

Seizures

Seizures may be due to idiopathic epilepsy or the presence of an irritating focus, such as a neoplasm or an infectious process. There are two types of epilepsy: (1) generalized seizures