Diseases of the Nervous System

Clinical Neuroscience and Therapeutic Principles

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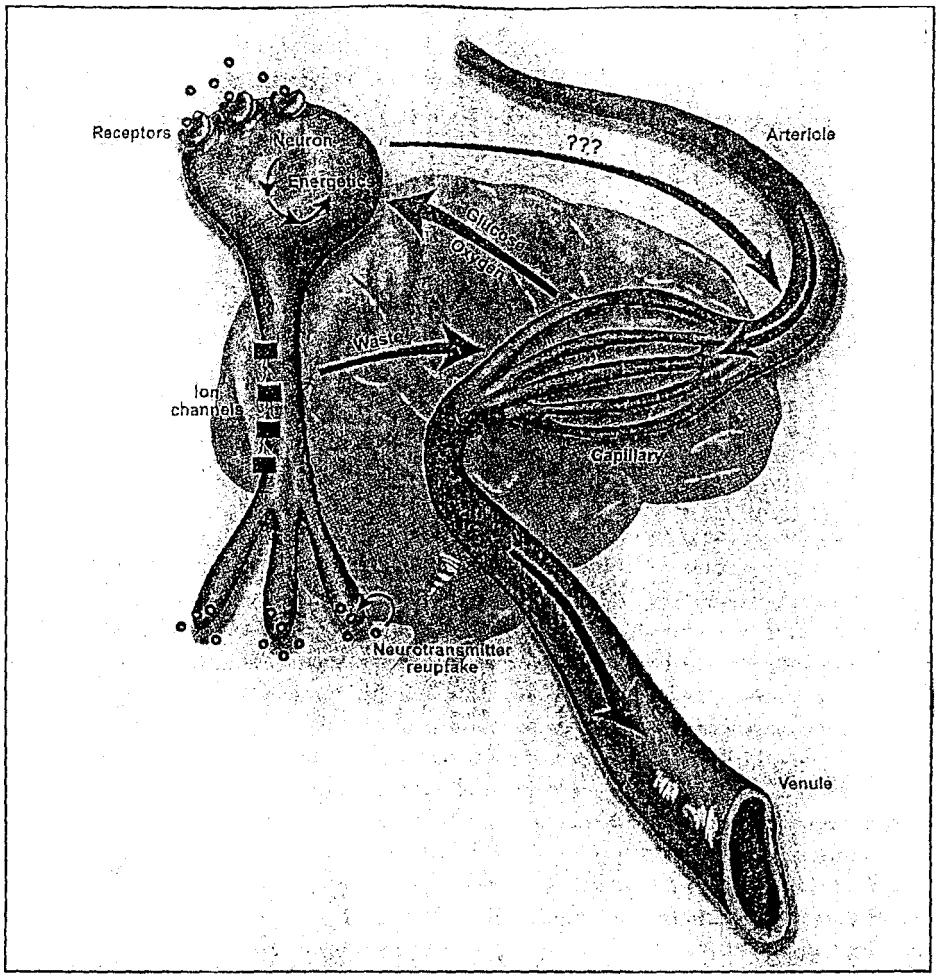

Fig. 10.1. Schematic diagram illustrating the physiological mechanisms which can be visualized by functional imaging, Brain function is represented by a neuron that receives synaptic input, conducts electrical signals by an energy dependent process, and has synaptic output with transmitter recycling. The adjacent microvasculature provides oxygen and glucose to support these functions through perfusion, which also affects local blood volume and blood oxygenation.

to fully characterize the mechanisms and mediators of AFC (Villringer & Dirnagl, 1995). The extent to which non-neuronal constituents of brain parenchyma contribute to the overall metabolic rate is also uncertain, and may be variable. Nonetheless, regional blood flow changes have typically colocalized with known functional specialization.

Functional imaging using radioactive tracers; PET and SPECT

The techniques of PET and SPECT enable the three-dimensional distribution of a radioactively labeled tracer to be measured in vivo. Radioisotopes used in PET imaging decay with the emission of positrons, which travel only a short distance in tissue before annihilating with an electron to form two colinear photons, each with 511 keV energy. In contrast, SPECT tracers emit just a single gamma ray, with energies dependent on the specific radioisotope used. The technology for detecting these gamma rays differs between the two systems, with PET generally having superior spatial resolution and system sensitivity, although SPECT is considerably less expensive, and much more widely available.

The spatial resolution of PET is limited by the range of positrons in tissue, and the slight acolinearity of the emitted gamma rays. Depending on the radioisotope, the absolute limit of resolution is approximately 1.5-2.5 mm, though generally this is not achieved in routine clinical practice. SPECT resolution is limited by the design of the

Table 10.1. Selected radiotracers for PET and SPECT imaging of the brain

Measurement	PET tracers	SPECT tracers
Cerebral blood flow	$H_2{}^{15}0$	[^{123}I)IMP, [^{99m}Tc]HMPAO, [^{99m}Tc]ECD
Cerebral blood volume	$^{11}C0$, $C^{15}0$	[^{99m}Tc]red blood cells
Oxygen metabolism	$^{15}O_2$	
Glucose metabolism	^{18}FDG	
Dopamine D_1 receptors	[^{11}C]SCH23390, [^{11}C]NNC756	[^{123}I]TISCH
Dopamine D_2 receptors	[^{11}C)raclopride, [^{11}C]NMSP	[^{123}I]IBZM, [^{123}I]IBF, [^{123}I]epidepride
Dopamine synthesis	(^{18}F) Dopa	
Dopamine transporters	[^{11}C]cocaine, [^{11}C]ß-CIT, [^{11}C]FP-CIT	[^{123}I]ß-CIT, [^{123}I]FP-CIT [^{123}I]IPT [^{99m}Tc]TRODAT,
	[^{11}C]CFT [^{11}C]methylphenidate	[^{123}I] altropane
Serotonin 5-HT_{1a}, receptors	[^{11}C]WAY100635, [^{18}F]MPPF	
Serotonin 5-HT_{2a} receptors	[^{11}C]MDL100907	[^{123}I]R-91150
Serotonin transporters	[^{11}C] (+)McN5652	[^{123}I]ß-CIT, [^{123}I]5-iodo-6-nitroquipazine, [^{123}I]IDAM,
		[^{123}I]ADAM
GABA receptors	[^{11}C] flumazenil	[^{123}I[iomazenil
NMDA receptors	[^{18}F]AFA	[^{123}I)MK801, [^{123}I]CNS1261
Nicotine receptors	[^{11}C] nicotine	[^{123}I]nicotine
Opioid receptors	[^{11}C]carfentanil, [^{11}C]diprenorphine	
Gene expression	[^{18}F]FIAU, (^{18}F]FGCV	[^{123}I]FIAU
Brain tumours (various types and modes *of* action)	^{18}FDG, [^{11}C]methionine, [^{11}C]thymidine	^{201}Tl [^{123}I]MIBG, [^{111}In]octreotide

collimator, and the distance from the subject to the detector. Most clinical systems can attain a resolution of 6-7 mm, though better resolution is possible with more specialized collimators. The temporal resolution of both systems is poor, as it can take several minutes of scanning to acquire sufficient statistics to form an image. However, despite the poorer spatial and temporal resolution of PET and SPECT compared with other modalities, such as fMRI, their tremendous advantage is their exquisite sensitivity. PET and SPECT can measure picomolar (10^{-12}) concentrations of tracer, many orders of magnitude less than can be detected with MRI. The quantity of radiotracer injected is tiny, and generally has no effect an the biological system under study.

Radiotracers for PET and SPECT

Many radioisotopes for PET imaging are found naturally in living organisms and are amenable to labeling biologically interesting molecules. These include carbon (^{11}C), nitrogen (^{13}N), oxygen (^{15}0), and fluorine (^{18}F). SPECT radioisotopes tend to be much larger, such as technetium (^{99m}Tc) and iodine (^{123}I), and are more difficult to incorporate into a radiotracer without disturbing the biochemical properties of the molecule. However, SPECT tracers generally have longer half-lives, and are therefore much more widely available than PET radioisotopes, which usually require an on-site cyclotron and production facility. Applications of these imaging technologies have gone hand-in-hand with developments in radiopharmaceutical chemistry. Both PET and SPECT are now capable of imaging biological systems with unprecedented accuracy and sensitivity, mainly due to the tremendous advances in the development of novel radiopharmaceuticals (Table 10.1).

Cerebral blood flow and metabolism

Originally, PET and SPECT were used to measure cerebral blood flow and metabolism. A number of tracers exist which can measure regional cerebral blood flow (rCBF), such as [^{123}I]IMP, [^{99m}Tc]HMPAO and [^{99m}Tc]ECD for SPECT, and $H_2{}^{15}0$ for PET. The SPECT tracers are examples of the `trapping' mechanism for measuring cerebral function. For a molecule to enter the brain, it must be neutral