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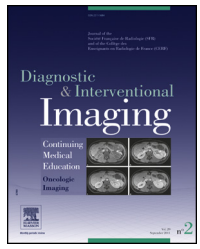

CONTINUING EDUCATION PROGRAM: FOCUS...

Functional imaging of cerebral perfusion

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Abstract The functional imaging of perfusion enables the study of its properties such as the vasoreactivity to circulating gases, the autoregulation and the neurovascular coupling. Downstream from arterial stenosis, this imaging can estimate the vascular reserve and the risk of ischemia in order to adapt the therapeutic strategy. This method reveals the hemodynamic disorders in patients suffering from Alzheimer's disease or with arteriovenous malformations revealed by epilepsy. Functional MRI of the vasoreactivity also helps to better interpret the functional MRI activation in practice and in clinical research.

Reminders about cerebral perfusion

The study of cerebral perfusion provides critical information to understand the functioning of the central nervous system and apprehend its dysfunction, among the main causes of morbidity and mortality in the West. In neurology and psychiatry, the identification of these microvascular pathophysiological disorders may provide information that may help to better characterize a several diseases, or even assess individual vulnerability.

Above all, cerebral perfusion allows for the transfer of appropriate quantities of glucose and oxygen for the functional needs of the brain, while eliminating heat and some catabolites such as CO_2 [1]. Perfusion is a dynamic physiological phenomenon able to respond to changes in the homoeostasis of the vascularized organ and the entire body. Like any biological function, general and local factors are likely to not only modify its state of equilibrium but also its adaptive properties. This adjustment is both passive, due to the

Abbreviations: ASL, arterial spin labeling; BOLD, blood oxygenation level dependent; CBF, cerebral blood flow; CBV, cerebral blood volume; CVR, cerebral vasoreactivity; fMRI, functional MRI; MRA, magnetic resonance angiography; P_aCO_2, arterial pressure in CO_2; P_eCO_2, expiratory pressure in CO_2.

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mechanical characteristics of blood vessels, and active by the arteriolar vasomotricity. The vasomotricity controls the caliber of the arterioles, so as to maintain the blood supply during variations in neuronal activity (neurovascular coupling), cerebral perfusion pressure (autoregulation), capnia, oxygenation and pH (vasoreactivity) [1].

Cerebral perfusion may simply be characterized by the cerebral blood flow (CBF), defined by the volume of blood transiting by the mass of the cerebral parenchyma per unit of time (classically expressed in ml/100 g of cerebral parenchyma/min). Since the density of brain tissue is close to that of water, the mass is often converted into volume, allowing the CBF to be expressed as a percentage of the parenchyma perfused per second (s^{-1}) (Table 1). The direct measurement of this dynamic property is especially difficult. This has given rise to the development of multiple, more or less invasive, methods that can, more or less, be considered in man. Numerous indicators and analytic models, with their advantages and disadvantages, have thereby been proposed [1,2]. The initial methods, such as those developed by Kety and Schmidt with the inhalation of NO_2 [3], measured a global CBF based on the analysis of the concentration of the marker at the entry and exit from the vascular system. In imaging, the CBF is measured on the scale of a cerebral region (rCBF), or even the pixel of a digital image and the voxel with tomography techniques. The success, over the last decades, of the imaging that has been established due to a major reduction in the invasiveness of the procedures and an increase in the temporal and spatial resolutions, has led to assimilate the rCBF with the CBF.

The cerebral blood flow and the cerebral blood volume (CBV) are two physiologically, closely related parameters, since they depend on the variations in arteriolar resistance. The mechanics of the fluids proportionally links variations in the volume with the square root of variations in flow. In the neurosciences, this ratio is estimated by: $([V/Vo] = [F/Fo]^{\alpha})$ Vo and Fo representing the volume and flow at the initial state, and V and F the volume and flow at the final state. With an experimental modulation of the cerebral perfusion by CO_2, α was estimated as being close to 0.40 in the animal [4–6]. In man, values of α between 0.29 and 0.73 have been reported with high regional disparities [7,8]. These heterogeneities are likely to reflect differences between the methods of measurement [9], the regional variability of the capillary density [10,11], the physiological mechanism used to modulate the perfusion [7,12,13], the time interval between the early variations in the CBF that are mainly based on the arteriolar and capillary sectors, and later variations in the CBV that better reflect the venous sector [6,14,15].

Table 1 Basal cerebral perfusion values usually admitted in man [1].

Mean CBF	≅60 ml/100 g/min ≅60 ml/100 ml/min (parenchyma density = 1.04 g/ml) ≅1 ml/100 ml/s ≅0.01/s (or 1% of the parenchyma corresponds to the fresh blood each second)
CBF grey matter	80 ml/100 g/min
CBF white matter	20 ml/100 g/min
Density grey matter / Density white matter	≅1
CBV	4 ml/100 g ≅4% of the parenchyma ≅60 ml of blood for a 1500 g brain
Arterial / capillary / venous CBV [280]	21% / 33% / 46%

Physiological variations in cerebral perfusion

At rest, the cerebral perfusion decreases with age [16] and is significantly higher in women [17]. The cerebral perfusion is closely related to the activity of the brain. It is often measured in the neurosciences and in medicine since it reflects the interaction between the vessels and the neurons through neurovascular coupling. Moreover, the cerebral perfusion is maintained roughly constant in order to deal with variations in the blood pressure and intracranial pressure by autoregulation. The cerebral perfusion is also sensitive to variations in the arterial concentration in CO_2 and O_2 by the vasoreactivity (Fig. 1). All of these physiological functions are based on the vasomotricity that enables, through the dilation and contraction of the vessels, to adjust the cerebral blood flow in order to guarantee the cerebral activity by dealing with the general and local physiological constraints [18].

Innervation of cerebral vascularization

Extrinsic innervation

The extrinsic vascular innervation of the pial arteries arrives from the peripheral nervous system by the upper cervical, sphenopalatine, trigeminal and optical ganglions that relay the information from peripheral baroreceptors. The extrinsic innervation is mainly sympathetic vasoconstrictor (noradrenalin, serotonin, neuropeptide Y) and parasympathetic vasodilator (acetylcholine, nitric oxide, VIP). The arteries progressively divide into arterioles that enter the cerebral parenchyma. They consist of an internal layer of endothelial cells, smooth muscle cells and an outer layer of leptomeningeal cells that form the external tunic. The arteriole is separated from the parenchyma by the Virchow-Robin space that contains the cerebrospinal fluid and is bordered by astrocytes on the outside. As the arterioles enter the parenchyma, the fluid space disappears and the arterioles and then the capillaries are in direct contact with the feet of the astrocytes that form the glia limitans [19–21].

Intrinsic innervation and the neurovascular unit

The intrinsic innervation of the intra-parenchymatous arterioles by the central nervous system relies on cortical interneurons and the efferences of subcortical neurons