Applied cerebral physiology

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Abstract

The brain uses large amounts of glucose for its basal energy requirements, and these are further increased during cerebral activation. In order that glucose can provide this energy, a plentiful and uninterrupted supply of oxygen is necessary. Cerebral blood flow is therefore critical for normal cerebral function. Its control is dictated by local intrinsic metabolic needs as well as extraneous factors such as arterial blood pressure, arterial carbon dioxide and oxygen tension, temperature and neural factors. This article reviews cerebral metabolism and cerebral blood flow and techniques by which both can be monitored.

Keywords Cerebral autoregulation; cerebral blood flow; cerebral metabolism; intracranial pressure

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Learning objectives

After reading this article, you should understand the:

- importance of an uninterrupted supply of oxygen and glucose for normal cerebral metabolism
- fundamentals of the regulation and measurement of cerebral blood flow
- concept of intracranial pressure and how it affects cerebral perfusion pressure

Cerebral metabolism and blood flow

The primary function of the brain is to generate neuronal action potentials in response to stimulation. The movement of ions against electrical gradients and the release and regeneration of neurotransmitters at synapses are central to this process. These functions require a large amount of energy in the form of adenosine triphosphate (ATP). Under normal conditions, the metabolic fuel is almost exclusively glucose and an appropriate supply of oxygen is needed for the oxidative process. This article outlines the mechanisms by which the brain receives its vital supply of glucose and oxygen and how it balances these against demands (Table 1).

Cerebral metabolism

The brain consumes more energy than any other tissue in the body. Glucose is the brains main energy source. Cerebral metabolic rate for glucose (CMRGl) is about 30 mg/100 g/minute, approximately 25% of the body's total glucose consumption. The majority of this energy is used to maintain ion gradients across neuronal membranes via the Na^+/K^+-ATPase ion pumps. Glucose crosses the blood–brain barrier via the GLUT 1 transporter and then enters cells via the appropriate glucose transporter (i.e. GLUT 1 to astrocytes, GLUT 3 to neurons and GLUT 5 to microglial cells).

Under normal aerobic conditions, glucose contributes to tricarboxylic acid (TCA) cycle and oxidative phosphorylation to provide ATP for energy. The remainder is converted to amino acids, proteins and lipids. Under hypoxic conditions the glucose receptors are upregulated. Glucose is anaerobically metabolized by glycolysis to form lactate, which is converted to pyruvate in neurons and which can then be used in the TCA cycle. Lactate can be actively removed across the blood–brain barrier via a monocarboxylate transporter. During fasting the brain utilizes ketone bodies (exported from the liver) and are broken down to acetyl coenzyme A (acetyl-CoA), which is oxidized via the TCA cycle to yield energy. Gluconeogenesis can also occur in such conditions. If cerebral blood flow (CBF) ceases, glycogen reserves can be exhausted within 2 minutes. Hypoglycaemia results in cerebral cellular dysfunction, manifesting as anxiety and confusion, convulsions and eventually coma.

Cerebral blood flow (CBF)

Normal aerobic cerebral metabolism requires uninterrupted supply of oxygen. About 70% of the total CBF is supplied by the carotid arteries and the rest via posterior pair vertebral arteries. These anterior and posterior circulations are joined at the circle of Willis in the base of the brain and this anastomosis is incomplete in 50% of individuals.

The brain receives 15% of the cardiac output (750 ml/minute in adults) and resting CBF is approximately 50 ml/100 g/minute (Table 1). Being more metabolically active, grey matter has a greater blood flow per minute, receiving 90 ml/100 g/minute compared to 20 ml/100 g/minute in white matter. Consequently grey matter has greater cerebral metabolic rate for oxygen ($CMRO_2$) (Table 1).

A reduction of CBF to approximately 20 ml/100 g/minute results in a loss of consciousness within seconds. Brain cell death (infarction) takes place at about 3 hours with flows of 10 ml/100 g/minute and after 30 minutes.

Cerebral perfusion pressure (CPP)

The perfusion pressure of the brain is dependent on the pressure difference between the driving pressure or mean arterial pressure (MAP) and the intracranial pressure (ICP) – the pressure that needs to be overcome to supply adequate blood to the brain. This pressure difference is known as the CPP. A normal CPP is 70–80 mmHg; the threshold for critical ischaemia is 30–40 mmHg. Even at normal levels of MAP, an elevated ICP of more than 20 mmHg will compromise CPP. This emphasizes the importance of

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Normal cerebral physiological values

CBF	750 ml/minute or 15% of cardiac output
CBF (global)	50 ml/100 g/minute
Grey matter	90 ml/100 g/minute
White matter	20 ml/100 g/minute
$CMRO_2$ (grey matter)	3 ml/100 g/minute
$CMRO_2$ (white matter)	1 ml/100 g/minute
CMRGl (global)	30 mg/100 g/minute or 25% of total body consumption

CBF, cerebral blood flow; $CMRO_2$, cerebral metabolic rate for oxygen; CMRGl, cerebral metabolic rate for glucose.

Table 1

maintaining an adequate MAP in circumstances such as head injury to ensure adequate perfusion.

Cerebral Perfusion Pressure = Mean Arterial Pressure − Intracranial Pressure

Intracranial pressure

The contents of the skull are brain parenchyma (80%), blood (9%), CSF (6%) and interstitial fluid (5%). Normal intracranial pressure is believed to be 7–12 mmHg. ICP is a dynamic pressure and fluctuations occur with arterial pulsations, position, respiration, coughing and straining (Figure 1). The Monroe–Kellie doctrine states that because intracranial volume is fixed, an increase in volume of one of the components contained within the skull, unless accompanied by a reduction in volume of the other components, will lead to a rise in ICP. Initially, as the brain volume increases, compensation occurs by movement of CSF into the spinal compartment, accompanied by a reduction in cerebral blood volume. However, as the compensatory mechanisms are overwhelmed, ICP rises dramatically with just small increases in intracranial volume (Figure 2). Severely raised ICP will cause brainstem compression with hypertension, bradycardia and irregular respiration (Cushing's reflex).

Surgical methods of reducing ICP may include CSF drainage or decompression. Reduction of intracranial blood volume can be achieved medically by reducing arterial carbon dioxide tension ($PaCO_2$), which promotes cerebral vessel vasoconstriction, or by increasing venous drainage with a head-up position and by providing adequate sedation and muscular relaxation, which reduces intrathoracic. Interstitial fluid volume reduction can be achieved by fluid restriction or by the administration of diuretics or corticosteroids.

CSF

CSF is an ultrafiltrate of plasma that circulates freely throughout the cerebral ventricles bathing the brain and spinal cord. It is formed at the rate of about 500 ml/day. If the rate of formation of CSF exceeds the rate of reabsorption (e.g. if blockage of the CSF circulation is present) hydrocephalus occurs.

Traditionally, CSF flow was thought to be directional, being produced from the choroid plexuses and circulating through cerebral ventricles, around the spinal cord and the subarachnoid spaces and ultimately being reabsorbed by subarachnoid villi into the cerebral venous sinuses (see Cerebrospinal Fluid and its Physiology, on pages 611–612 of this issue).

Dynamic intracranial pressure (ICP) trace

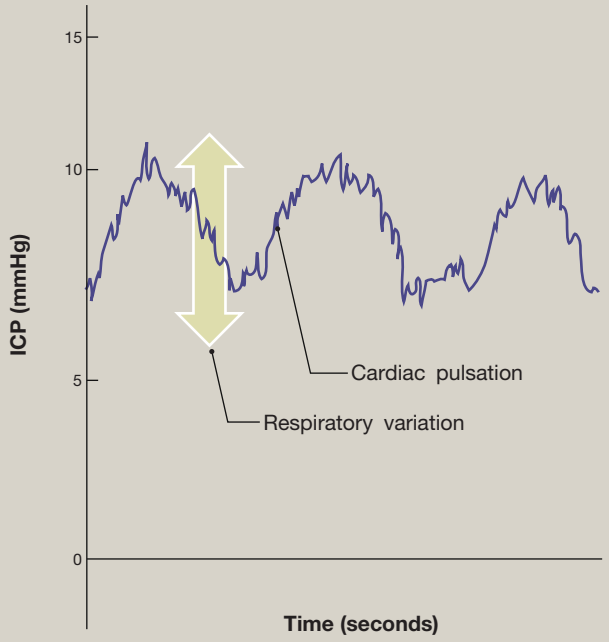
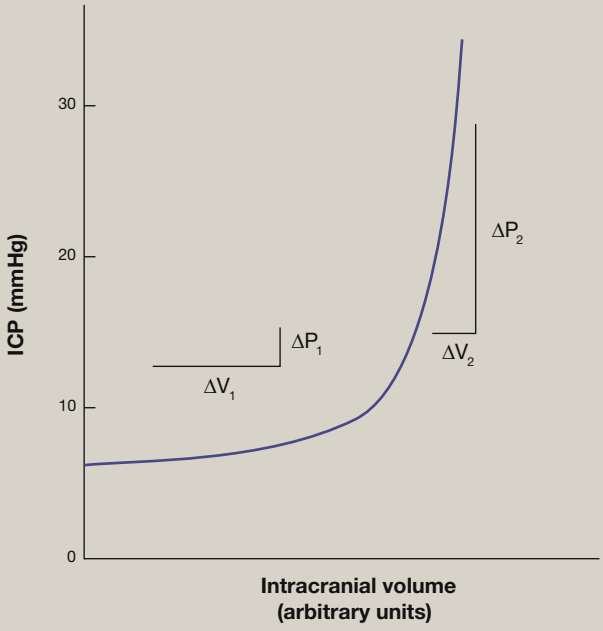


Figure 1

Intracranial pressure–volume curve



ICP, intracranial pressure; P, pressure; V, volume.

Figure 2