Continuing Education in Anaesthesia, Critical Care & Pain Advance Access published March 1, 2013

Cerebral physiology

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Revalidation FOR ANAESTHETISTS
RCA Revalidation matrix
Matrix reference 1A01, 1A02, 3F00

Key points

The brain is enclosed in a rigid box with a fixed volume and an increase in the volume of any of its constituents will lead to an increase in intracranial pressure (ICP).

The volume of venous blood in the cerebral vasculature is small but very important as it can provide immediate compensation for increases in ICP.

The cerebrospinal fluid provides the largest compensation for raised ICP but changes occur slowly.

Volatile anaesthetic agents increase the ratio of cerebral blood flow and cerebral metabolism.

Maintaining sufficient cerebral blood flow to meet metabolic demands after a neurological insult is important to prevent secondary (ischaemic) brain injury.

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The brain is a very complex organ which needs a continuous delivery of oxygen and nutrients. To sustain consciousness, satisfactory perfusion and adequate oxygen delivery is vital but it is equally essential to maintain a constant supply of glucose as the brain has virtually no stores of glucose. Loss of consciousness ensues within seconds of ischaemia secondary to a reduction in cerebral blood flow (CBF), with permanent brain damage occurring with 3–8 min of insufficient blood supply.[1] The brain also has a unique heterogeneous structure with areas of variable blood supply that is directly related to its function and metabolism.

Cerebral blood volume

The brain receives its blood supply from the internal carotid and vertebral arteries (Fig. 1) which drain via the cerebral veins and dural venous sinuses into the internal jugular veins. The volume of blood in the whole brain is small and contained mainly in the venous sinuses and pial veins. The grey matter is composed of the cell bodies of the neurons which are involved with the complex functions of the human body and hence requires a larger proportion of the arterial blood supply. On the other hand, the white matter is essentially composed of axons which transmit impulses in between the neurons. As it is involved with less complicated functions than the grey matter, it needs a smaller fraction of the blood supply.

Cerebral blood flow

Although the brain constitutes only 2% of body mass (1400 g), it receives a large proportion (12–15%) of the resting cardiac output in the adult.

The CBF is best described by the Hagen–Poiseuille equation for laminar flow, which demonstrates a direct relationship between flow, cerebral perfusion pressure (CPP), and calibre of cerebral vessels:

$$\mathrm{CBF} = \frac{\pi \Delta P r^4}{8\,\mu l}$$

where π is the mathematical constant, ΔP the pressure gradient which is the CPP, r the radius/calibre of blood vessel, μ the dynamic viscosity of blood, and l the length of the blood vessel.

CBF will thus improve if the CPP increases and the cerebral vasculature is vasodilated.

Cerebral perfusion pressure

Perfusion pressure is the difference in the pressures between the arterial and venous circulation which dictates the blood flow to the organ. In the brain, the perfusion pressure or the CPP is affected by another pressure within the skull [i.e. intracranial pressure (ICP) explained below]. In pathological conditions, if the ICP is increased, the flow through the cerebral blood vessels can be restricted.

In adults,

$$\mathrm{CPP} = \mathrm{MAP} - (\mathrm{CVP} + \mathrm{ICP})$$

where MAP is the mean arterial pressure and CVP the central venous pressure.

In normal adults, the CPP is variable, usually ranging between 70 and 90 mm Hg and the CBF is constant. When the CPP decreases below 50 mm Hg, there is an increased risk of brain ischaemia affecting the electrical activity in the brain.

The cerebrovascular resistance (CVR) is essentially the hindrance to the CBF determined predominantly by the calibre of the vessels. When cerebral vasodilatation occurs, the increase in the radius of the vessels not only decreases the CVR but also augments CBF. On the other hand, vasoconstriction of the cerebral vasculature will decrease CBF by increasing the CVR.

Cerebral metabolic rate

The cerebral metabolic rate (CMR) is the rate at which the brain utilizes metabolic substrates [e.g. oxygen ($CMRO_2$), glucose (CMR_{glu}), or generates by-products, e.g. lactate (CMR_{lact})]. The brain has the highest metabolic requirements

doi:10.1093/bjaceaccp/mkt001
Continuing Education in Anaesthesia, Critical Care & Pain | 2013

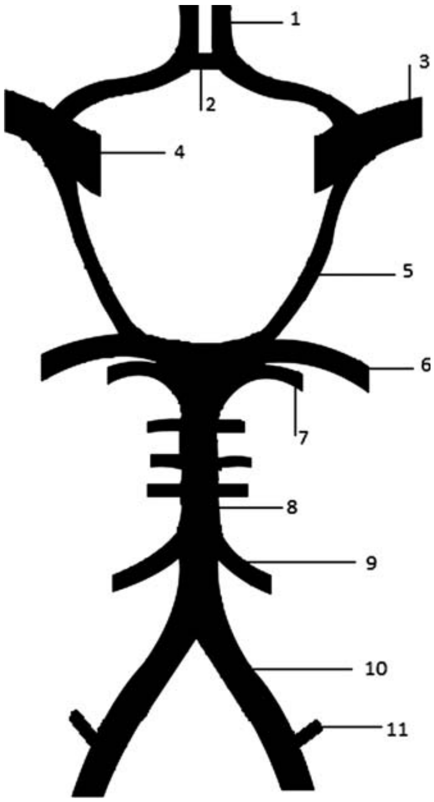

Fig 1 Arterial supply of the brain (Circle of Willis). 1: Anterior cerebral artery. 2: Anterior communicating artery. 3: Middle cerebral artery. 4: Internal carotid artery. 5: Posterior communicating artery. 6: Posterior cerebral artery. 7: Superior cerebellar artery. 8: Basilar artery. 9: Anterior inferior cerebellar artery. 10: Vertebral artery. 11: Posterior inferior cerebellar artery.

of any organ in the body which is reflected by its high blood flow. The brain oxygen consumption accounts for 20% of basal oxygen consumption (~50 ml min^{-1}) at rest and relies, almost completely, on oxygen-dependent metabolism of glucose for energy production:

$$CMRO_2 = CBF \times (A - V)O_2 \text{ content difference}$$

where A is the cerebral artery and V the cerebral veins.

Because CBF is adjusted to meet the metabolic demand, oxygen by the grey matter is approximately five times more than by the white matter.

Glucose is not only the main energy substrate for the brain but also a precursor for neurotransmitters, including γ-aminobutyric acid, glutamate, and acetylcholine, and is essential to maintain a constant CBF and therefore the substrate supply. Under aerobic conditions, oxidative phosphorylation produces 38 molecules of ATP for every molecule of glucose. Sixty per cent of the energy produced is utilized for the functioning of the neurons (i.e. their chemical and electrical activity), and the other 40% to maintain the integrity and homeostasis of the neuronal cells.[2] The brain has very limited capacity for anaerobic metabolism and under these conditions, one molecule of glucose undergoes glycolysis to produce only two molecules of ATP. The lactate produced anaerobically is utilized to carry out the fundamental processes essential to maintain the cell structure. Aerobic metabolism is restored if perfusion is re-established immediately, otherwise permanent cell death follows. For values of cerebral blood volume, cerebral blood flow and cerebral metabolic rate of oxygen and glucose in normal adults, see Table 1.

Table 1 Average values in normal healthy individuals

	Grey matter	White matter	Average (whole brain)
CBV (ml per100 g tissue)	4–6	1.5–2.5	3.5–4.5
CBF (ml per 100 g tissue per min)	100–110	20–25	45–55
$CMRO_2$ (ml per 100 g tissue per min)	4–4.5	0.7–1.0	3–3.5
CMR_{glu} (mg per 100 g tissue per min)	6.5–8.5	1.2–2.2	4–5

Intracranial pressure

The concept of ICP can best be understood if we compare the brain to a 'closed box' or a fixed and rigid container. The Monro–Kellie hypothesis states that the volume of the brain and its constituents inside the bony cranium is fixed and cannot be compressed. To preserve a constant pressure in the box, the volume of the contents inside must be maintained.[3]

The intracranial contents can be theoretically divided into three compartments:

(i) brain volume ≈ 85%,
(ii) cerebrospinal fluid (CSF) ≈ 10% (150 ml) and
(iii) blood ≈ 5% (50–75 ml).

In adults, ICP is normally 5–15 mm Hg when supine and is posture-dependent, being lowest in the upright position. Increase in ICP above a critical level is not tolerated because it results in a decrease in the CPP of the brain and can also cause local compression of brain tissue against the tentorium, falx, and foramen magnum and ultimately herniation.

Control of ICP

There are many ways that ICP is controlled.

Volume buffering (pressure–volume relationship)

Blood and CSF provide the main protection to the brain when the intracranial volume increases. There is an initial compensation which prevents major changes in the intracranial compliance with minimal increases in ICP. In the presence of intracranial pathology, the volume of one component within the cranium increases (e.g. haematoma, brain swelling) and, when the compensatory mechanisms are exhausted, there is a marked increase in ICP with a reduction in CPP and cerebral ischaemia (Fig. 2).

Blood, despite being the smallest volume compartment within the cranium, has the most significant role in compensation for ICP changes as the cerebral venous volume can be changed very