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Brain vascular and hydrodynamic physiology

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ABSTRACT

Protecting the brain in vulnerable infants undergoing surgery is a central aspect of perioperative care. Understanding the link between blood flow, oxygen delivery, and oxygen consumption leads to a more informed approach to bedside care. In some cases, we need to consider how high we can let the partial pressure of carbon dioxide go before we have concerns about risk of increased cerebral blood volume and change in intracranial hydrodynamics. Alternatively, in almost all such cases, we have to address the question of how low can we let the blood pressure drop before we should be concerned about brain perfusion. This review provides a basic understanding of brain bioenergetics, hemodynamics, hydrodynamics, autoregulation, and vascular homeostasis to changes in blood gases, which is fundamental to our thinking about bedside care and monitoring.

Protecting the brain in vulnerable infants undergoing surgery is a central aspect of perioperative care. Understanding the link between blood flow, oxygen (O_2) delivery, and O_2 consumption will lead to a more informed approach to bedside care. For example: What are the limits to normality? How do we know when a significant perturbation has occurred? What preventive measures can we take to protect the brain? This brief review is not going to be able to answer these questions, as we are still in the dark ages in regard to differentiating between cause and effect. Rather, it will provide a basic understanding of brain bioenergetics, hemodynamics, hydrodynamics, autoregulation, and vascular homeostasis to changes in blood gases, which is fundamental to our thinking about bedside care and monitoring. Each section will start from what we know in man and identify relevant information in neonates.

Brain bioenergetics

The brain is one of the most metabolically active organs of the body and it requires a constant supply of O_2 and nutrient, mainly glucose.[1] In an adult, the brain consumes about one-fifth of total body O_2 utilization. Cerebral metabolic rate for oxygen ($CMRO_2$) in normal, conscious, young men is approximately 3.5 mL O_2/100 g brain per min. The $CMRO_2$ by an entire adult brain of an average weight (i.e., 1.4 kg) is therefore about 50 mL O_2/min. A 70-kg adult consumes about 250 mL O_2/min in the basal resting state. Therefore, the brain, which represents only about 2% of total body weight, accounts for 20% of the resting total body O_2 consumption.

The functions of nervous tissues are mainly excitation and conduction of nerve impulses, and these are reflected in the increasing activity of the brain. Electrical energy, ultimately, is derived from chemical processes, and it is likely that most of the energy consumption of the brain is used for the active transport of ions. Oxygen is used in the brain almost entirely for the oxidation of carbohydrates. The energy equivalent of the total cerebral metabolic rate is, therefore, approximately 20 W or 0.25 kcal/min. Let us assume that this energy is used mainly for the synthesis of high-energy phosphate bonds, the efficiency of the energy conservation is approximately 20%, and the free-energy hydrolysis of the terminal phosphate of adenosine triphosphate (ATP) is 7 kcal/mol. This energy expenditure supports the steady turnover of close to 7 mmol, or approximately 4×10^{21} molecules, of ATP per minute in the entire brain.

In the normal, *in vivo*, state, glucose is the only significant substrate for energy metabolism in the brain. The stoichiometry of glucose utilization and $CMRO_2$ is as follows. The normal, conscious human brain produces carbon dioxide (CO_2) at about the same rate of $CMRO_2$ of 156 μmol/100 g tissue per min leading to a respiratory exchange ratio of 1. $CMRO_2$ and CO_2 production are equivalent to a rate of glucose utilization of 26 μmol/100 g tissue per min, assuming 6 μmol of O_2 is consumed and CO_2 is produced for each μmol of glucose completely oxidized to CO_2 and water. (The actual glucose utilization is, however, 31 μmol/100 g/min. For complete oxidation of glucose, the theoretical ratio of O_2:glucose utilization is 6; the excess glucose utilization is responsible for a measured ratio of only 5.5 μmol O_2/μmol glucose. The fate of the excess

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glucose is unknown but, probably, is distributed in lactate, pyruvate, and other intermediary metabolites.)

Development and cerebral glucose metabolism

Cerebral glucose utilization in 5-week-old infants is three-quarters that of an adult brain. The developing brain also metabolizes lactate, ketone bodies, amino acids, and free fatty acids. Adult rates of glucose utilization are first achieved by the age of 2 years; after this age, there is a further increase through to the age of 8 years, followed by a decline in metabolic rate through to the age of 20 years. This crescendo–decrescendo pattern of change likely represents the consequence of brain development and subsequent "pruning" of neurons, synapses, and pathways that occurs with maturation.[2]

Cerebral oxygen kinetics

Human brain maturation is incomplete at birth and continues to progress during the first years of life. As already discussed, brain development is associated with regional changes in glucose metabolism. Given that O_2 needs to be delivered to the tissue at a rate that is biochemically proportionate to metabolic needs, it should come as no surprise that regional cerebral blood flow (CBF) also changes with development.

$CMRO_2$ must be equal to the total amount of O_2 delivered to cerebral tissue per unit time minus the amount leaving in the venous circulation per unit time and the amount that accumulates in the cerebral tissue per unit time (Eq. (1), Table). The extraction of O_2 from cerebral tissue is so closely matched to the brain's metabolic needs that the O_2 content of brain tissue is small. The vast majority of the arteriovenous O_2 difference ($AVDO_2$) is made up of O_2 off-loaded from hemoglobin, and the amount of O_2 off-loaded from hemoglobin in the cerebral circulation is tightly regulated by many physiologic factors including brain pH, brain temperature, concentration of cerebral metabolites, and amount of adult hemoglobin.

Cerebrovascular hemodynamics

CBF at birth is, on an average, 50 mL/100 g/min, increasing after birth to a maximum of 70 mL/100 g/min at 5 years, and then decreasing to reach adult levels after 19 years. The global CBF represents more than 50% of cardiac output at the peak value around 1–3 years of age, indicating why this age group is at risk for cerebrovascular catastrophes consequent to perioperative systemic disorders.

Table
Equations describing the pathway for blood and oxygen in the brain.

Equations	
$CMRO_2 = (CBF \times CaO_2) - (CBF \times CvO_2) - CiO_2$	(1)
$Q = \Delta P / R$	(2)
$Q = (p \times r^4 \times \Delta P)/(8\eta \times L)$	(3)
$Q = CBV/t'$	(4)
$CBV = 1.09 \times CBF^{0.29}$	(5)
$OEF = (SaO_2 - SjvO_2)/SaO_2$	(6)
$OEF = CMRO_2/(CBF \times 1.34 \times [Hb] \times SaO_2)$	(7)

CaO_2 = oxygen content of arterial blood; CBF = cerebral blood flow; CBV = cerebral blood volume; CiO_2 = oxygen content of brain tissue; $CMRO_2$ = cerebral metabolic rate for oxygen; CvO_2 = oxygen content of venous blood; Hb = hemoglobin concentration; η = blood viscosity; L = vessel length; OEF = oxygen extraction fraction of brain; OEF = oxygen extraction fraction of brain; ΔP = pressure gradient between inflow and outflow; Q = flow; R = resistance to flow; r = vessel radius; SaO_2 = oxyhemoglobin saturation of arterial blood; $SjvO_2$ = oxyhemoglobin saturation of jugular venous blood; t' = mean transit time of blood.

Under physiologic conditions, CBF is closely coupled to the O_2 requirements of the tissue. $CMRO_2$, in turn, depends on the density of neurons and on their state of functional activation. CBF, therefore, differs in different species and with different types of anesthesia; it is higher as the brain is smaller (because neurons are more closely packed) and as the level of anesthesia is shallower. Typical flow rate of CBF of the cerebral cortex in adults in the awake-state is 80 mL/100 g/min. Under anesthesia, CBF decreases by about 20%, and under deep general anesthesia by up to 50%. In white matter, blood flow is about 25% of that of the cortex in the awake-state, but it is not markedly influenced by anesthesia; differences between white and gray matter diminish when subjects are deeply anesthetized.

The physical laws that describe steady laminar flow of uniform fluids through non-distensible tubes are helpful in understanding *in vivo* cerebrovascular hemodynamics. Ohm's law predicts that flow is proportional to the pressure gradient between inflow and outflow divided by the resistance to flow (Eq. (2), Table). In brain, cerebral perfusion pressure (CPP) is taken as the driving pressure for CBF. CPP is the difference between intra-arterial pressure and the pressure in the thin-walled veins, collapsible at the point of entry into the venous sinuses. Venous pressure changes in parallel with intracranial pressure (ICP) and is normally 2–5 mmHg higher than ICP. Therefore, the driving pressure is calculated as the difference between mean arterial pressure (MAP) and the cerebral venous pressure or ICP, whichever is higher. Resistance is determined principally by vessel radius and can be calculated from Eq. (2), (Table) to estimate total cerebrovascular resistance (CVR) or resistance of any vascular segment of interest in which flow and upstream and downstream pressure gradients are known. Poiseuille's law shows that the major determinants of CBF are perfusion pressure, blood viscosity, and vessel radius (Eq. (3), Table). Vessel length is an unchanging parameter.

Cerebral blood volume

Cerebral blood volume (CBV) is determined by two factors, CBF and capacitance vessel diameter (i.e., small veins and venules). CBV increases with vasodilation and decreases with vasoconstriction. Although CBF frequently changes in the same direction as CBV, these variables are inversely related under normal situations (e.g., autoregulation) or in pathological situations. Further, blood volume is not equally distributed throughout brain; blood volume per unit weight is greater in gray than in white matter, with further variation among the various nuclei. Average CBV in humans is 3–4 mL/100 g tissue. Pathology, which affects either CBF or cerebral venous capacitance, may modulate CBV with subsequent effects on ICP. More quantitatively, the central volume principle relates the volume that intravascular blood occupies within brain (CBV [mL]) and the volume of blood that moves through the brain per unit time (CBF [mL/min]) (Eq. (4), Table). For example, although CBV is increased during vasodilation, CBF may not change if blood flow velocity is correspondingly reduced. Surplus blood volume accumulates primarily within cerebral veins, known to receive sympathetic innervation and to respond to sympathetic stimulation, and within capillaries to a smaller degree. Normally, increases in CBV can be physiologically controlled by two maneuvers: increased blood outflow to the extracranial venous circulation and restricted inflow via constriction of the major feeding arteries.

Cerebral vascular supply and drainage

The arterial blood supply to the brain comes from two circulations, anterior and posterior. The anterior circulation of the brain arises from the internal carotid artery, to middle cerebral artery