Non-invasive monitoring of cerebral tissue oxygenation in vivo by near infrared spectroscopy: a sensitive indicator of oxygenation changes

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Introduction
Near infrared spectroscopy (n.i.r.s.) is a relatively new method for the non-invasive monitoring in vivo of changes in the haemoglobin saturation level and the redox state of cytochrome aa₃, the terminal enzyme of the respiratory chain [1]. The n.i.r.s. method has previously been described [2, 3], and the validity of the technique was demonstrated by studies on isolated organs and preliminary studies on the intact brain in vivo (rat and rabbit) [4, 5]. The results presented here indicate that n.i.r.s. is a very sensitive indicator of changes in the oxygenation level of haemoglobin and of the redox state of cytochrome aa₃ in the rat brain in vivo.

Materials and methods
The method of n.i.r.s. [6] and instrumentation has been described previously [3]. The system drift was less than 0.004 absorbance/h for all four laser diodes. The baseline variation was less than 4% of the signal induced by mild hypoxic changes and less than 2–3% for complete oxygenation changes. Male adult rats (Wistar), weight 300–600 g, were anaesthetized with fentanyl (0.07 mg) and Fluanisone (0.02 mg) intramuscularly, tracheotomized and artificially ventilated with 100% oxygen and with a p₁₀₂ of 398 and a p_c₁₀₂ of 25 mmHg. The oxygen content of the ventilating gas was reduced to 21% at which time the p₁₀₂ was 96 and p_c₁₀₂ 26 mmHg. N.I.R.S. measurements [Fig. 1] showed a lag phase followed by an increase in the level of deoxyhaemoglobin and a simultaneous decrease in the level of oxyhaemoglobin. The cyt aa₃ signal was unaffected. The animal was not hypoxic, the pH and p_c₁₀₂ were unaltered and there was no affect on the cardiovascular parameters. The oxygen content was then increased to 100%; the n.i.r.s. recordings showed an increase in the level of oxyhaemoglobin to a greater level than previously recorded with a simultaneous fall in the level of deoxyhaemoglobin and to a lower amount than initially. These results are consistent with a luxury perfusion. The p₁₀₂ was determined to be 402 mmHg. The cerebral blood volume trace showed an increase on readministration of the 100% oxygen, which is consistent with the luxury perfusion and increase in the level of oxyhaemoglobin to compensate for its previous reduction. The desaturation of haemoglobin observed upon decreasing the oxygen from 100% to 21% could be due to the anaesthetic agents (since it would be expected to be saturated in air). The results are consistent with data presented on the effect of pentothal on the oxygenation level of haemoglobin [11]. This has been suggested to be due to a resetting of the equilibrium level of oxy/deoxyhaemoglobin, owing to a shift in the haemoglobin–oxygen dissociation curve.

In the second series of studies, extreme hypoxia was induced followed by recovery [Fig. 2]. Transmission studies were made on a rat head and the animal was ventilated with 100% oxygen, with a p₁₀₂ of 446 and p_c₁₀₂ of 19.4 mmHg. Measurements were made continuously before, during and

Abbreviations used: n.i.r.s., near infrared spectroscopy.

Results
Several series of rat cerebral transmission studies were performed including (a) oxygenation change without hypoxia occurring and with no effect on pH or carbon dioxide levels; (b) extreme hypoxia followed by recovery.

One of a series of rat cerebral transmission studies is described and shown [Fig. 1]. The rat was artificially ventilated with 100% oxygen and with a p₁₀₂ of 398 and a p_c₁₀₂ of 25 mmHg. The oxygen content of the ventilating gas was reduced to 21% at which time the p₁₀₂ was 96 and p_c₁₀₂ 26 mmHg. N.I.R.S. measurements [Fig. 1] showed a lag phase followed by an increase in the level of deoxyhaemoglobin and a simultaneous decrease in the level of oxyhaemoglobin. The cyt aa₃ signal was unaffected. The animal was not hypoxic, the pH and p_c₁₀₂ were unaltered and there was no affect on the cardiovascular parameters. The oxygen content was then increased to 100%; the n.i.r.s. recordings showed an increase in the level of oxyhaemoglobin to a greater level than previously recorded with a simultaneous fall in the level of deoxyhaemoglobin and to a lower amount than initially. These results are consistent with a luxury perfusion. The p₁₀₂ was determined to be 402 mmHg. The cerebral blood volume trace showed an increase on readministration of the 100% oxygen, which is consistent with the luxury perfusion and increase in the level of oxyhaemoglobin to compensate for its previous reduction. The desaturation of haemoglobin observed upon decreasing the oxygen from 100% to 21% could be due to the anaesthetic agents (since it would be expected to be saturated in air). The results are consistent with data presented on the effect of pentothal on the oxygenation level of haemoglobin [11]. This has been suggested to be due to a resetting of the equilibrium level of oxy/deoxyhaemoglobin, owing to a shift in the haemoglobin–oxygen dissociation curve.

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Abbreviations used: cyt. aa₃, cytochrome aa₃; HbR, HbO₂, deoxygenated and oxygenated haemoglobin, respectively.

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Effect of dibutyryl cyclic AMP on bile acid synthesis in biliary-drained rats

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Previous experiments in our laboratory and others have shown that bile acid synthesis in isolated hepatocytes is increased in the presence of dibutyryl cyclic AMP and glucagon [1-3]. In addition, there is evidence from studies in vitro that the activity of cholesterol 7α-hydroxylase, the rate-limiting enzyme in bile acid synthesis [4-6], may be modulated by a phosphorylation–dephosphorylation mechanism [7, 8]. These findings suggest strongly that cyclic AMP may have a role in the regulation of bile acid synthesis. No previous work, however, has examined the effect of cyclic AMP on bile acid synthesis in vivo.

In this study, we have investigated the effect of dibutyryl cyclic AMP on bile acid synthesis in biliary-drained rats,

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