Introduction

The regulation of cerebral blood flow (CBF) is mainly attributed to myogenic mechanisms and metabolic influences. The myogenic reaction to intraluminal pressure is considered to provide cerebral autoregulation (8), whereas pCO2 tension and tissue lactate level are assumed to regulate regional cerebral blood flow (rCBF) according to metabolic requirements (7, 10). The means by which regulation of local cerebral microcirculation (ICBF) occurs, however, remains unknown (12).

After brain lesion, it is generally held that vasogenic edema reduces the CBF and impairs cerebral oxygen supply, and the main objectives of treatment are therefore to increase CBF and oxygenation. However, brain damage is associated with many biochemical derangements, including release of neurotransmitters and local mediators and disturbances of the ion homeostasis in the tissue. Disturbances of cerebral metabolism and vasomotor control after brain damage which are not yet clarified thus acquire significance for therapy and prognosis.

We therefore investigated the relation between local oxygen metabolism and microflow in normal brain cortex, following vasogenic edema, and following calcium antagonistic treatment.

Material and Methods

Measurement of Oxygen Metabolism and ICBF

Local cortical tension (tpO2), local metabolic rate of oxygen (lCMRO2), and ICBF were measured with a polarographic multiwire surface electrode. In contrast to preliminary experiments (13), tpO2 was measured with Au electrodes, each 15 μm thick, which give a more stable polarographic plateau than Pt wires (5). In addition, four 100-μm Pt electrodes were encased in the same glass electrode for measuring tissue hydrogen tension (pH2); these Pt wires were palladinated before each investigation (6). These signal electrodes were surrounded by an Ag/AgCl reference electrode divided into two separate semicircular parts. Using different polarization voltages this integrated electrode allowed a simultaneous record of oxygen and hydrogen tension; the tpO2 was measured in the stable plateau at −750 mV and remained unaffected by the simultaneous pH2 record at +100 mV.

The electrode was prepared with Teflon membrane as described in (13) and counterbalanced during recording to avoid any pressure on the cortex.
tpO₂ was measured continuously; lCBF was measured by H₂ clearance at
intervals. At the end of each experiment, lCMRO₂ was approximated by
the decrease in tpO₂ following sudden and complete CBF arrest. The
CBF interruption was achieved by inflating a cervical cuff balloon up
to 400 mmHg, after which the EEG proved to be isoelectric within 4–6 s.

**Animals, Anesthesia, Injury, Treatment**

We used male SPD rats weighing 250–340 g randomized into groups of at
least eight animals:

The "normal animals" (control group) were anesthetized with 65 mg/kg
sodium pentobarbital or 320 mg/kg ketamine hydrochloride and trepanned
between the coronal, sagittal, and lambdoid sutures (breathing sponta-
neously). pO₂, lCBF and lCMRO₂ were measured on the right cortex.

The injured animals were further randomized into three groups. In
anesthesia with sodium pentobarbital a standardized cold brain injury
was produced as described previously (4). Either 24, 48, or 72 h after
trauma, these animals were trephined and oxygen metabolism and lCBF
were measured in the perifocal edematous area outside the necrosis
as well as over the opposite, "collateral" hemisphere.

The treatment group was trepanned 24 h after injury, and during record-
ing of pO₂ and lCBF, nimodipine (Nimotop) was infused at 20 µg/kg/min
via the tail vein.

In all animals, blood gases, systemic arterial pressure (femoral arte-
ry), and body temperature were measured in addition.

**Evaluation**

All measurements were evaluated on-line with computer (Intertechnique
IN 110, 16 channel A/D converter):

tpO₂ was plotted as a histogram (Figs. 1–4), and histogram statistics
(arithmetic mean, median, mode, skewness, curtosis) calculated.

The lCBF measurement started with the rats breathing a mixture of 8%
H₂, 20% O₂, and 72% N₂; after saturation of the tissue with H₂ (stable
plateau) the gas mixture was changed to air. The H₂ clearance curve
was approximated by the regression function:

\[ tpH₂(t) = A \cdot e^{-b \cdot t} \]  

With t in min, b directly equals lCBF in ml/100 g/min (12).

The time constant of the electrode is too high for direct measurement
of lCMRO₂ from pO₂ clearance after circulatory arrest. The clearance
curve was therefore corrected by the computer according to:

\[ 0 = \frac{dpO₂_{meas}}{dpO₂_{real}} \cdot (a' \cdot \frac{AdpO₂_{real}}{-b/1}) - dpO₂_{real} \]  

This formula was derived from step response of the electrode after
DIRAC impulse (2, 12).