Blood flow and oxygen utilisation in the contralateral cerebral cortex of patients with untreated intracranial tumours as studied by positron emission tomography, with observations on the effect of decompressive surgery

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SUMMARY Using positron emission tomography, regional cerebral blood flow and oxygen utilisation were measured in the contralateral cortex of 14 patients with a variety of intracranial tumours. A comparison was made with cortical values derived from 14 normal controls. Compared with normal subjects, patients with brain tumours had a significant reduction in oxygen utilisation and blood flow in their contralateral cortex. Decompression resulting from craniotomy and biopsy, led to a partial reversal of this cerebral hypofunction.

With the advent of positron emission tomography (PET) it has become possible to measure, quantitatively, regional cerebral blood flow and a variety of metabolic processes in man non-invasively.¹⁻³

Most of the workers in the PET field who have studied the pathophysiology of intracerebral tumours have compared the values obtained for flow and metabolism in the tumour with that of contralateral "normal" brain.^{4,5} In some studies it was noted that intracerebral tumours were associated with a depression of oxygen metabolism and blood flow in the overlying ipsilateral cortex compared to contralateral cortical tissue.^{5,6} Ito demonstrated a reduction in cortical blood flow in the contralateral cortex of patients with brain tumours compared with that in a group of normal controls, but did not demonstrate a significant difference in cortical oxygen utilisation.⁵ Other workers have demonstrated a suppression of glucose metabolism in ipsilateral grey matter remote from the tumour compared with contralateral grey matter.⁷ The ipsi-

lateral findings demonstrate the undercutting effect that a neoplasm has on cortical physiology.

We have suspected for some time that an intracranial tumour may profoundly affect not only blood flow but oxygen utilisation in the contralateral supposedly normal brain. This study was undertaken to clarify the situation in man, using PET. The aim of the study was two-fold and both parts dealt with regional blood flow and oxygen utilisation in cortical tissue only. Firstly a comparison was made between the physiology of the contralateral cortex of brain tumour patients and that of normal controls. Patients on steroid therapy were excluded from the study as it has been shown that the administration of dexamethasone to patients with brain tumours is associated with a reduction in cortical blood flow and regional blood volume as measured by the oxygen-15 steady-state technique (Leenders *et al*, in preparation). Most of the published PET work dealing with regional blood flow and metabolism in cerebral tumour patients to date has included patients on steroid therapy. In the second part of this study the effect of cerebral decompression on the physiology of the contralateral cortex was studied in patients who underwent craniotomy with complete or partial excision of their tumour.

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PET scanning of brain tumour patients

Table 1 Relevant data on the brain tumour patients

Patient	Sex	Age (yr)	Diagnosis	Level of scan cms above OM line	Drugs
1	M	55	Astrocytoma (Grade I)	+7	Phenytoin 300 mg daily
2	M	60	Astrocytoma (Grade IV)	+6	Nil
3	F	39	Astrocytoma (Grade I)	+7	Phenytoin 400 mg daily
4	F	56	Brain metastasis (Colon)	+6	Paracetamol
5	M	44	Astrocytoma (Grade II)	+7	Nil
6	F	55	Brain metastasis (Breast)	+7	Nil
7	F	76	Brain metastasis (Lymphoma)	+6.5	Nil
8	M	29	Astrocytoma (Grade III)	+7	Carbamazepine 200 mg tds
9	F	63	Astrocytoma (Grade IV)	+6.5	Paracetamol
10	M	59	Astrocytoma (Grade II)	+7	Nil
11	M	49	Astrocytoma (Grade IV)	+7	Nil
12	M	27	Astrocytoma	+7	Phenytoin 300 mg daily
13	F	75	Brain metastasis (Breast)	+6.5	Nil
14	M	63	Pineal gland tumour	+6.5	Nil

Patients and methods

Details of the 14 patients with intracranial tumours are given in table 1. The mean age of this group was 54 years (SD 15, range 27 to 76). The control group consisted of 14 normal volunteers. The mean age of this group was 48 (SD 11, range 35 to 64). There was no significant difference in the mean age, haemoglobin, stable oxygen content or PCO₂ of the arterial blood between these two groups. Details of the seven patients examined before and after surgery are given in table 2.

The purpose and nature of this study was approved by the Hammersmith Hospital Research Ethics Committee. The United Kingdom Administration of Radioactive Substances Advisory Committee gave permission for the administration of the radionuclides used in this study. The written informed consent was obtained from all participants. Radiation dosimetry has been described in detail elsewhere.² For a two plane study the lung dose is approximately 2500 mrem.

The oxygen-15 steady-state inhalation technique has been dealt with in detail by Frackowiak *et al.*² The extended version that corrects for intravascular ¹⁵O as described by Lammertsma *et al.*⁶ was used in this study. Regional cerebral blood flow (rCBF), oxygen extraction ratio (rOER, that is the fraction of oxygen extracted from the arterial blood), oxygen utilisation (rCMRO₂), and regional blood volume (rCBV) were measured. The scanning

procedure and the method used to correct for signal attenuation due to tissue absorption have been described previously.^{2,4}

In brief PET permits the absolute measurement of the regional tissue concentration of the positron emitting radionuclides ¹⁵O and ¹¹C within a transaxial slice of the brain. Tracer equations have been formulated that accurately describe the fate of ¹⁵O when it is inhaled sequentially in the form of C¹⁵O₂ and ¹⁵O₂. The only prerequisite to the use of these operational equations is that the inhaled tracers be delivered continuously at a constant rate during the study. By measuring the concentration of the ¹⁵O within the tissues using PET and in the arterial blood (withdrawn during scanning), using a cross-calibrated well counter, these tracer kinetic equations can be solved and rCBF, rOER and rCMRO₂ calculated in absolute units. Labelling of red cells by inhaling ¹¹CO provides a means of measuring regional cerebral blood volume.¹⁰

The patients were scanned with an ECAT II (EG & G Ortec) PET scanner.^{11,12} Medium resolution shadow shields were used giving a transaxial resolution of 17 × 17 mm (FWHM) and a slice width resolution of 16 mm (FWHM). To ensure a constant position, a grid of light was projected onto the patients forehead onto which washable ink marks were placed at appropriate points. Any movement by the patient was immediately noted on a closed circuit television and rapid, accurate repositioning was ensured. Each plane was scanned for 5 minutes during

Table 2 Relevant data on patients who underwent surgery. The Hb and PCO₂ values were those taken during the pre- and post-op scans

Patient	Sex	Age (yr)	Diagnosis	Surgical procedure	Drugs	Haemoglobin (g)		PCO ₂ (kpa)		Time of second scan (days post-op)
						Preop	Postop	Preop	Postop	
I	M	63	Meningioma	Craniotomy and complete excision	Dexamethasone	15.0	11.1	4.6	4.9	5
II	F	26	Haemangioblastoma	Craniotomy and open biopsy	Nil	12.5	12.9	4.8	4.9	7
III	M	28	Astrocytoma Grade II to III	Posterior fossa exploration and biopsy	Dexamethasone	14.2	12.2	5.2	5.6	14
IV	F	19	Astrocytoma Grade II	Craniotomy and open biopsy	Dexamethasone	12.5	13.5	4.5	4.8	12
V	M	45	Astrocytoma Grade IV	Craniotomy and open biopsy	Brufen	13.5	11.5	4.9	5.1	7
VI	F	47	Metastasis	Craniotomy and subtotal excision	Nil	12.4	9.2	4.8	5.0	21
VII	M	62	Astrocytoma Grade II	Craniotomy and excision biopsy	Dexamethasone	11.5	11.4	4.7	4.7	6

Fig 1 (a) Line diagram showing the anatomy of the brain at the level 6.5 ± 0.5 cms above and parallel to the orbito-meatal line. (b) The $rCMRO_2$ scan with region of analysis (ROI) blocks displayed.

which between 1 and 2 million coincident events were recorded, during the $C^{15}O_2$ and $^{15}O_2$ emission scans. To facilitate multiple and painless arterial blood sampling during the scan, a 22 gauge Teflon cannula was inserted into the radial artery under local anaesthesia. This cannulation was only performed after patency of the ulnar artery was confirmed by Allen's test. Multiple arterial samples are necessary to ensure that the tracer equations are solved using values that are indeed representative of a steady-state. If a steady state was not achieved, the study was rejected. Two planes were studied, the first through the plane of the tumour and a second at a level of OM + 6.5 cms when the tumour was outside this plane. The latter level provides a relatively uniform ribbon of cortex for analysis. All participants were scanned in a quiet resting state.

Data analysis

The plane chosen for analysis in the first part of this study was 6.5 ± 0.5 cm above and parallel to the orbitomeatal line. This plane includes central white matter in the centrum semiovale and peripheral cortical grey matter (see fig 1a). Attention was restricted in this study to the ribbon of cortex. Since the resolution of the scanner used was $17 \times 17 \times 16$ mm (FWHM) and the width of the cortical ribbon is appreciably less than this, the values given for cortex in this study will be "contaminated" by the inclusion of a substantial amount of white matter. This results in lower values being obtained for cortical function than would be expected if only pure grey matter were sampled. The plane chosen for analysis in the pre- and post-craniotomy study was at the level of the tumour, as defined by an X Ray transmission CT scan.

A computer program based on a method previously described¹³ was used to provide a "cortical plot" consisting of rectangular regions 15×7.5 mm in size arranged contiguously around the peripheral ribbon of cortex. Each region contained eighteen 2.5×2.5 mm pixels. This ribbon was defined from the peripheral rim of high oxygen utilisation evident in the $rCMRO_2$ image. These rectangular regions of interest (ROIs) were positioned so as to minimise the standard deviation between individual pixel values for $rCMRO_2$. This produced the greatest homogeneity in cortical tissue being sampled (see fig 1b).

Results

Figure 2a shows the X-ray CT scan of a patient with a grade III astrocytoma in the left frontal region. Figure 2b shows the PET images of CBF, OER, $CMRO_2$ and CBV calculated for the same plane. The tumour corresponds to the region of reduced $rCMRO_2$ and $rOER$. This was a consistent finding in every tumour studied, confirming previous reports.^{5,6}

Values of contralateral cortical $rCBF$, $rOER$, $rCMRO_2$ and $rCBV$ obtained from the 14 brain tumour patients and 14 controls are shown in table 3 and portrayed in the form of a dot diagram in fig 3.

Fig 2 Images from a patient with a grade III astrocytoma (not included in this study as the patient's dose of dexamethasone was changed after operation). (a) Conventional X-ray CT scan of the brain showing a poorly enhancing tumour in the left frontal region. (b) The PET (rCBF, rOER, rCMRO₂ and rCBV) images through the same plane. The tumour region is represented by the area of low rCMRO₂, rCBF and rOER.

The mean contralateral cortical rCMRO₂ of the patient group (2.7 ± 0.5 ml of O₂/100 ml/min) was significantly lower than that in the normal group (mean 3.1 ± 0.4 ml of O₂/100 ml/min), $p < 0.025$. The rCBF in the patient group (mean 32.8 ± 6.7 ml/100 ml/min) was also significantly lower than that of the control group (mean 43.7 ± 7.7 ml/100 ml/min) $p < 0.001$. The two groups were not exactly age-matched, the mean age of the patient group being slightly higher than that of the control group. There is some evidence to suggest that cortical rCBF and to a lesser extent rCMRO₂ decline with age.¹⁴ In our control group there was no correlation with rCBF and age but a slight trend with rCMRO₂. After allowing for this trend with age, using an analysis of covariance the difference in rCMRO₂ was still significant ($p < 0.05$). There was no significant difference in the mean rOER and rCBV between the two groups.

Figure 4a shows the enhanced X Ray CT scan of a patient with a recurrent meningioma in the right parietal region. Figure 4b shows similarly scaled PET images of rCBF, rOER and rCMRO₂ for the same patient before and after surgery. These demonstrate an increase in both rCBF and rCMRO₂ following decompression. The data obtained for all seven patients in the second part of the study are shown in table 4 and portrayed in the form of a dot diagram in fig 5. The significant findings were an increase in both mean rCMRO₂ and mean rCBF for the contralateral cortex of the tumour patients after surgery. The mean oxygen utilisation rose from a value of (2.45 ± 0.49) to (2.86 ± 0.27) mls of O₂/100 ml/min ($p < 0.05$) (a mean rise of 17% CMRO₂). The mean rCBF value rose from 28.0 ± 5.2 to 37.9 ± 11.9 ml/100 ml/min ($p < 0.05$) a mean rise of 35% CBF. No significant change was noted in the mean rOER and rCBV before and after surgery. However as expected, in those patients who had a rise in rCBF in excess of metabolic requirements the rOER fell. In patient VII the rise in rCBF was inadequate to meet the increased metabolic demand and the rOER rose to 0.70 (normal range 0.35–0.47).

Discussion

The first part of this study demonstrated a significant depression of mean oxygen metabolism and blood flow in the contralateral cortex of patients with brain tumours compared to mean cortical function in normal controls. The reasons for such a depression in the tumour group may be related to several factors: the increased intracranial pressure associated with some brain tumours, transneuronal depression (crossed "cerebral diaschisis"), or a general "toxic"

Table 3 Absolute "cortical" values for rCBF, rOER, rCMRO₂ and rCBV in both tumour and normal control groups

Patient	Tumour group				Controls	Normal group			
	rCBF*	rOER	rCMRO ₂	rCBV‡		rCBF*	rOER	pCMRO ₂ †	rCBV‡
1	43.2	0.41	3.35	3.5	1	47.1	0.40	3.46	4.4
2	34.9	0.48	3.03	3.4	2	44.3	0.46	3.64	4.1
3	40.2	0.36	2.57	3.9	3	43.8	0.40	3.12	4.3
4	34.2	0.47	2.77	5.7	4	40.9	0.42	2.88	3.7
5	39.8	0.43	3.74	4.7	5	45.6	0.44	3.90	3.5
6	32.1	0.52	2.86	4.8	6	34.3	0.45	3.15	3.3
7	38.2	0.41	2.43	3.7	7	37.5	0.46	2.88	4.0
8	32.1	0.43	2.43	4.3	8	43.0	0.42	3.10	4.2
9	32.7	0.50	2.74	3.2	9	67.2	0.29	3.31	3.5
10	20.0	0.52	1.63	3.2	10	39.4	0.39	2.74	3.1
11	34.3	0.41	2.62	4.6	11	41.8	0.43	2.72	3.7
12	35.2	0.36	2.62	4.1	12	42.2	0.48	3.36	4.8
13	27.8	0.55	2.52	3.1	13	47.3	0.43	2.51	3.8
14	25.0	0.47	2.40	4.0	14	37.5	0.40	2.89	4.0
Mean	32.8	0.45	2.69	4.0	Mean	43.7	0.42	3.12	3.9
SD	6.7	0.06	0.49	0.8	SD	7.7	0.05	0.39	0.5

*ml/100 ml/min.
†ml of O₂/100 ml/min.
‡ml/100 ml.
Significant difference in rCBF (p < 0.001) and rCMRO₂ (p < 0.025) unpaired t test.

effect of the tumour on cerebral metabolism. Early studies on brain tumour patients by Kety *et al*¹⁵ showed that a rise in CSF pressure above 33 mm Hg was associated with a definite decrease in global CBF. The lowest CBF values were found in the patients with the highest CSF pressure. All of Kety's patients with a CSF pressure greater than 35 mm Hg however were comatose and it was likely that CSF

pressures in our patient group (although not measured) were lower than this. Shenkin demonstrated that a brain tumour confined to one hemisphere did not specifically affect the CBF and CMRO₂ of the hemisphere but had effects on the whole brain.¹⁶ Hoedt-Rasmussen and Skinhoj¹⁷ studied two patients with hemispheric tumours (both without increased intracranial pressure) using the Krypton

Fig 3 Dot diagrams of rCBF, rOER, rCMRO₂ and rCBV. A comparison of values for contralateral cortex in the brain tumour group with cortical values from the normal control group.

Fig 4 (a) An enhanced X ray CT scan showing a large recurrent meningioma in the right parietal region. (b) Similarly scaled rCBF, rOER and rCMRO₂ PET images before and after surgery, showing an increase in rCBF and rCMRO₂ after excision of the tumour.

85 clearance method. They found that cerebral blood flow in both ipsilateral and contralateral hemispheres were similarly reduced. The effects of increased intracranial pressure on cerebral blood flow and oxygen utilisation have been examined experimentally in anaesthetised monkeys by Grubb *et al.*¹⁸ These workers raised the intracranial pressure (ICP) by infusing artificial CSF into the cisterna magna. They noted that increases in ICP up to 70

mm Hg caused a progressive rise in CBV without any fall in cerebral blood flow. With further increases in ICP up to 94 mm Hg, CBV remained elevated without change, while CBF declined significantly. They recorded no significant change in oxygen utilisation even at the highest pressure.

Unfortunately no attempt was made to measure the intracranial pressure in these patients so we have no estimate of cerebral perfusion pressure. All the patients were however fully conscious and co-operative. Tables 5 and 6 provide clinical and radiological details that may be useful in assessing the degree of increased intracranial pressure. We acknowledge that there may be wide fluctuations in the intracranial pressure of these tumour patients where compliance is very low, but in one separate tumour patient where intracranial pressure was only 26 mm Hg a profound depression in cortical rCMRO₂ was found. Such a finding, coupled with the results from Kety, Hoedt-Rasmussen and Grubb's studies, suggests that mechanisms other than raised ICP alone may be responsible for the fall in rCMRO₂ and rCBF in the contralateral cortex.

If only those patients with symptoms and signs of raised ICP or radiological evidence of mass effect, midline shift, contralateral hydrocephalus or obstructive hydrocephalus are considered, the depression of rCMRO₂ and rCBF in the contralateral cortex becomes even more significant (mean rCBF = 29.0 ± 5.8 , mean rCMRO₂ = 2.45 ± 0.42). Three of the tumour patients were taking phenytoin; the effect of this drug on rCBF and rCMRO₂ is being investigated at present but to date no significant effect has been demonstrated.

Kempinsky, using cats, demonstrated that an acute focal injury of the cerebral cortex resulted in a transient depressive effect upon the electrical activity of the contralateral cortex. He then showed that this depressive effect was dependent principally upon having an intact corpus callosum.¹⁹ He suggested that as impulses from one group of neurons can facilitate the activity of another group, any damage to such facilitatory neurons can lead to a depression of activity in remote dependant neurons. Whether the pathways in man pass directly through the corpus callosum or indirectly via the midbrain or the brain stem is not clear. The time course of haemodynamic alterations in the non-ischæmic hemisphere after an acute focal ischæmic injury has been examined by Slater *et al.*²⁰ They observed that the depression of CBF in the contralateral hemisphere was not maximal immediately but progressed gradually during the first week post infarction. These data suggest that acute neuronal depression secondary to disconnection from afferent stimulation cannot be the only cause of diaschisis, as has

Table 4 Values for rCBF, rOER, rCMRO₂ and rCBV before and after surgery

Patient	Pre operation rCBF*	rOER	rCMRO ₂ †	rCBV‡	Postoperation rCBF*	rOER	rCMRO ₂ †	rCBV‡
I	28.8	0.41	2.34	3.8	54.6	0.37	3.00	4.0
II	33.8	0.48	2.82	4.9	39.2	0.48	3.30	4.5
III	28.6	0.47	2.62	4.4	34.3	0.49	2.78	4.5
IV	27.0	0.62	2.88	3.9	28.0	0.58	2.94	4.0
V	24.3	0.51	2.05	3.7	32.5	0.48	2.47	3.7
VI	34.2	0.50	2.84	3.8	53.1	0.44	2.93	4.2
VII	19.4	0.52	1.58	3.2	23.9	0.70	2.62	3.3
Mean	28.0	0.50	2.45	4.0	37.9	0.51	2.86	4.0
SD	5.2	0.06	0.49	0.5	11.9	0.11	0.27	0.4

*ml/100 ml/min.
†ml of O₂/100 ml/min.
‡ml/100 ml.
Significant difference in rCBF and rCMRO₂ p < 0.05 (paired t test).

been postulated. Destruction or functional damage of neurones by a cerebral tumour itself, peritumoural oedema, or more remote pressure effects could lead to a reduction in neuronal activity in contralateral cortex by a similar mechanism.

The evidence for a general "toxic" effect of a tumour on cerebral metabolism remains mostly speculative. Although paraneoplastic syndromes (for example encephalomyelitis, dementia and subacute cerebellar degeneration) have been regularly recorded in association with non-cerebral tumours

their association with intracranial neoplasms has been poorly documented. Among the many proposed mechanisms, ranging from an autoimmune disorder to viral infection, is that of tumour production of biomolecules that may block neuroreceptor sites, which may in turn alter regional cerebral metabolism. If this were the case, then one might expect a reversal or partial reversal of any metabolic effect after excision or partial excision of the tumour.

A point that is often raised is whether the patients

Fig 5 Dot diagrams of rCBF, rOER, rCMRO₂ and rCBV. Measurements were taken before and after operation in seven patients. The significant changes were an increase in rCMRO₂ and rCBF after craniotomy.

Table 5 Clinical and radiological findings related to increased intracranial pressure

Patient	Symptoms suggestive of increased intracranial pressure	Papilloedema	CT scan changes suggestive of increased intracranial pressure
1	None	None	Comparatively mild mass effect slight midline shift
2	None	None	Peritumour oedema, no mass effect, no midline shift
3	None	None	Slight perifocal oedema. No mass effect
4	None	None	Slight midline shift with slight effacement of sulci ipsilaterally
5	None	None	None
6	None	None	Mass effect present. No midline shift
7	None	None	Perifocal oedema, no mass effect
8	None	None	Mass effect present. No midline shift
9	Headache and diplopia	YES	Mass effect and midline shift present
10	Headache	None	Marked peritumour oedema, mass effect and midline shift present
11	Headache and deteriorating visual acuity	YES	Mass effect and midline shift present
12	None	None	None
13	Headache vomiting ataxia		Mass effect and obstructive hydrocephalus present
14	Headache vomiting ataxia	Fundi not clearly seen	Mass effect and obstructive hydrocephalus present

and volunteers are in an equally quiet resting state during the scan. It is often expected that the patients being more motivated would be less anxious about undergoing this investigation than would normal controls. We were unable to detect any clinical difference in the level of anxiety between these groups. In addition if one accepts that hyperventilation with a lowering of $P_a\text{CO}_2$ may be a useful index of anxiety then again there was no difference between the two groups.

In the second part of this study it was shown that decompression by craniotomy and either partial or total excision of the tumour was associated with a partial reversal of this depression in metabolism and blood flow. This makes crossed "cerebral diaschisis" (a name usually reserved for the condition associated with infarcted brain) a less likely mechanism for the reduction in contralateral cortical $r\text{CMRO}_2$ as this would not be expected to reverse after craniotomy. If, however, one postulates that in addition to the tumour lesion itself there may be several other factors contributing to this transneuronal depression (for example perifocal oedema or pressure effects on more distal parts of the neurons) then

decompression could be associated with an increase in CMRO_2 and CBF. Shenkin *et al* demonstrated that six patients with brain tumours did not show a significant rise in CBF or oxygen metabolism when the intracranial pressure was lowered by direct ventricular drainage. Cerebral blood flow, however, did increase in response to the intravenous injection of 50% glucose.²¹ These workers attributed the beneficial effect of hypertonic glucose to haemodilution which resulted in a reduction of the arterial oxygen content, which in turn caused an increase in CBF. The increased CBF was thought to be more effective in removing metabolites. It is possible, however, that the hypertonic glucose could have altered CBF by other means (for example a reduction in perifocal oedema).

Two patients had a fall in haemoglobin after craniotomy. Such a fall would be expected to increase $r\text{CBF}$ but not $r\text{CMRO}_2$, and both these patients (I and VI) indeed showed the greatest increase in $r\text{CBF}$. The rise in $r\text{CBF}$ in these two patients was inappropriately high as judged by cortical metabolic requirements as a fall in $r\text{OER}$ occurred in both cases. The two patients (I and VII) who

Table 6 Clinical and radiological findings related to increased intracranial pressure

Patient	Symptoms suggestive of increased intracranial pressure	Papilloedema	CT scan changes suggestive of increased intracranial pressure
I	None	None	Considerable white matter oedema, mass effect, midline shift and contralateral hydrocephalus present
II	Headaches and diplopia	YES	Mass effect and slight obstructive hydrocephalus
III	Headaches, nausea and vomiting	YES	Mass effect and obstructive hydrocephalus
IV	Headaches and diplopia	YES	Considerable mass effect, midline shift and contralateral hydrocephalus
V	Headache and deteriorating visual acuity	YES	Considerable mass effect
VI	Headache and diplopia	YES	Peritumour oedema, considerable mass effect and midline shift
VII	Headaches	None	Mass effect, midline shift and contralateral hydrocephalus

had the greatest increase in $rCMRO_2$ were those where there was complete macroscopic excision of the tumour.

Only seven patients were scanned in the second part of this study and most were scanned at different times after surgery. There was no relation between the magnitude of postoperative change and the time of the second scan. The reproducibility for serial studies on an individual subject with this technique lies in the region of $\pm 10\%$. The changes in $rCBF$ and $rCMRO_2$ after craniotomy in the tumour group were greater than this and are unlikely to be artefactual. It is important to point out that none of the patients scanned postoperatively had deteriorated clinically. It is possible that if they had developed marked cerebral oedema after the procedure then the partial improvement in $rCBF$ and $rCMRO_2$ would probably not have occurred.

An interesting observation that we have not attempted to explain in this paper is the marked similarity in cortical $rCBV$ in both normals and patients. One would expect, on the basis of laboratory studies, a rise in $rCBV$ to maintain $rCBF$ as the cerebral perfusion pressure falls. In the absence of intracranial pressure monitoring we were unable to comment on the known complex relationship between $rCBF$ and $rCBV$ in these patients with space occupying lesions and raised intracranial pressure. The lack of a compensatory rise in cortical $rCBV$ in the tumour group is partly borne out by virtually no change in $rCBV$ post operatively.

In conclusion, compared with normal subjects, this group of patients with brain tumours had a reduction in oxygen metabolism and blood flow in their contralateral cortex. Decompression resulting from craniotomy and biopsy led to a partial reversal of this cerebral hypofunction. The reason for these findings are not clearly understood, but may be related in part to raised ICP, a general "toxic" effect of the tumour, or a focal effect of the tumour with any attendant oedema giving rise to a phenomenon similar to "crossed cerebral diaschisis".

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