Variations in Mean Cerebral Blood Flow under Anesthesia at Rest and During Cortical Activation


SUMMARY  More than one cerebral blood flow (CBF) measurement was performed on the same occasion in three groups of patients using the intracarotid \(^{133}\)Xenon technique. In the anesthetized group there was a highly significant reduction in CBF (mean = 24.3%) from the first to the second measurement. In those at rest under local anesthesia there was also a significant fall (mean 9.8%). The third group, who were stimulated during the second estimation, showed no change. A second CBF determination some time after beginning a study is recommended, especially in pharmacological studies, to provide a more reliable resting control, rather than the first value which represents flow in an "activated" brain which has not yet adapted fully to its new environment.

WHEN CEREBRAL BLOOD flow (CBF) is measured under general anesthesia (GA), it is important to be sure to what extent CBF may be influenced by the anesthetic agent used. Halothane, one of the most widely used inhalational anesthetic agents, was thought to reduce CBF\(^1\) but later work\(^2\) showed that— in common with most other inhalational anesthetic agents—it increases CBF. Intravenous barbiturates reduce CBF.\(^3\) However, the combination of induction by a short-acting intravenous barbiturate and maintenance by nitrous oxide has been reported as having a negligible effect.\(^4\) Since this provides too light a level of anesthesia for most purposes, phenoperidine or another neuroleptic analgesic—which has little apparent effect on CBF—\(^5\) is added during maintenance. This method is now widely used during measurement of CBF.

In a previous study\(^6\) we showed that when two measurements of CBF are separated by a short interval—\(\Delta PaCO_2\) and blood pressure remaining constant—there is a good correlation between them but the second is almost invariably lower than the first. The difference is particularly relevant when assessing the effect of drugs which cause short-term change in CBF; a consistent fall in CBF may lead to the vasodilator effect of a drug being underestimated.

Methods

All patients studied were undergoing carotid angiography for diagnostic purposes. Informed consent for CBF to be measured via the same carotid puncture was obtained from the patient.

Eleven patients (mean age 54 years) had two CBF measurements performed under GA under steady-state conditions; ten (mean age 43 years) had two measurements under local anesthesia (LA) also under steady-state conditions; ten (mean age 49 years) had two measurements under LA but were subjected to psychological stimulation during the second run.

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In the GA group, premedication was limited to atropine 0.6 mg subcutaneously. Induction was by intravenous methohexitone, approximately 0.88 mg/kg, suxamethonium 1 mg/kg and pancuronium 0.08 mg/kg. The patients were maintained on a Manley ventilator without rebreathing using two parts nitrous oxide to one part oxygen supplemented by carbon dioxide to achieve a PaCO\(_2\) close to 40 mm Hg. Phenoperidine 0.01 mg/kg was given intravenously after the suxamethonium and, if necessary, supplements of 0.005 mg/kg at half-hourly intervals. At the end of the procedure, the effects of pancuronium were reversed with neostigmine preceded by atropine. The level of anesthesia achieved was very light; patients woke within two minutes of stopping nitrous oxide. Patients to be studied under LA were given 60 mg of codeine phosphate and 12.5 mg of promethazine hydrochloride one hour beforehand.

After puncture of the common carotid artery the bifurcation was visualized in two planes by injection of small volumes of meglumine iothalamate (60% Conray 280) to a total of 8 to 10 ml. If no atheroma was present, a fine polythene catheter was introduced by the Seldinger technique and advanced up the internal carotid artery to the level of \(C1/C2\). To minimize the effect of the injection of contrast medium on CBF at least 20 minutes were allowed to elapse after visualization of the bifurcation before isotope was injected.\(^8\) Approximately 8 mCi of \(^{133}\)Xenon in 5 ml of saline were injected as a bolus. Fifteen regional detectors monitored the rate of clearance of the Xenon from the cerebral hemisphere.\(^7\) Analysis of the clearance curves by an on-line computer yielded a value for the flow over the first 2 minutes (\(F_{\text{initial}}\)). PaCO\(_2\) was measured before and during each CBF measurement and intra-arterial blood pressure was recorded intermittently via a pressure transducer connected to the carotid catheter. A CBF correction factor of 4% for each mm Hg difference was applied to the three cases in which the PaCO\(_2\) varied by more than 3 mm Hg.\(^9\) The corrected values are marked with an asterisk in the tables.

In the GA group, an 8 channel electroencephalogram (EEG), 4 channels symmetrically from each hemisphere, was recorded throughout on paper and magnetic tape. The tape...
record was subsequently computer-processed using a fast Fourier transform in 12 second epochs. The square roots of the 3–6 Hz power coefficients were summed for each epoch, to provide a data point representing the "EEG energy" in the 3–6 Hz band.10 The relatively few epochs containing obvious artifact on the paper record were replaced by a mean value between the epochs on either side of the artifact. The resulting data points were smoothed by a 7 point running average to yield graphs of energy in the 3–6 Hz band over the whole recording period from induction to recovery. The EEG paper trace was also surveyed by eye to detect any signs suggestive of a change in conscious level between the two periods of CBF measurement.

Patients in the GA and the first LA group were left entirely undisturbed during and between the CBF measurements. The patients in the second LA group were undisturbed until 30 seconds before the second estimation, when the neurological or psychological activity, listed in table 3, was commenced. Activity was continued throughout the 2-minute period of measurement.

Results

The mean CBF for both measurements under GA are shown in table 1. In four of the eleven cases the second flow was 40% less than the first. In six others it was reduced to a lesser degree and in only one was it the same. This reduction in CBF is highly significant (paired ‘t’ test p < 0.001), the mean fall in flow being 24.3% (SD = 15.3).

There was no significant change in the EEG energy between the two runs of CBF measurement in the eight cases with technically satisfactory recordings. Naked eye assessment of the tracings also showed no evidence of alteration in the level of consciousness between the two runs.

In the first group studied under LA eight of the ten patients had a lower CBF, one was unchanged and only one had a higher flow on the second run (table 2). The mean fall in flow for the group was 9.8% (SD = 9.9) this being significant at the 1% level (p < 0.01). In the second LA group subjected to neurological or psychological testing before and during the second run there was no significant change in the CBF level between the two runs (table 3).

Discussion

Our first hypothesis was that the reduction of CBF between the two measurements was due either to a deepening level of anesthesia or to the patient “falling asleep” under the anesthetic. The absence of change in the EEG, the rapid recovery of consciousness by the patients as soon as the anesthetic was stopped and the fact that a lesser, but considerable, fall in CBF was seen in patients under local anesthesia who were not asleep exclude these possibilities.

Our second hypothesis was that the CBF during the first run was increased as a result of the contrast medium injected to visualize the carotid bifurcation. However, it has been shown that the effect of small amounts of contrast medium on CBF does not persist for longer than eight minutes;4 CBF was not measured in our patients until at least 20 minutes had elapsed after injection.

Our final hypothesis is that the brain was not “at rest” at the time of the first measurement. The amount of stimulation caused by carotid catheterization, positioning the head and other maneuvers involved in the measurement of CBF, may have produced a state of “activation.” The lapse of further time between the first and second measurements without stimulation of any sort may have resulted in the brain becoming less active with a consequent decrease in CBF.

None of the patients examined under LA was particularly anxious during the study. The procedure had been explained to them beforehand, and every effort was made to make the atmosphere quiet and relaxed. Presumably, continued anxiety would have maintained CBF in the alert range. It is of particular significance that when the patient was alerted the EEG activity would have maintained CBF in the alert range. It is of particular significance that when the patient was alerted prior to the second run by neurological or psychological activity, the fall in CBF was no longer seen.

These findings have considerable implications for the interpretation of CBF measurement during psychological or pharmacological activation. It is usual in this type of experiment to make a base-line measurement of CBF and then, after an interval to allow for clearance of the isotope, to make a second measurement during administration of the stimulus to be tested. Our study suggests that once an individual has adapted to the experimental situation CBF will

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Table 1  Mean Cerebral Blood Flow Under General Anesthesia

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Diagnosis</th>
<th>Age</th>
<th>PaCO₂ Run 1</th>
<th>PaCO₂ Run 2</th>
<th>MABP Run 1</th>
<th>MABP Run 2</th>
<th>Mean Hosphere flow Run 1</th>
<th>Mean Hosphere flow Run 2</th>
<th>% change in CBF</th>
<th>EEG energy Run 1</th>
<th>EEG energy Run 2</th>
<th>% change in EEG energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dementia (multi-infarct)</td>
<td>53</td>
<td>40</td>
<td>40</td>
<td>100</td>
<td>85</td>
<td>30</td>
<td>26</td>
<td>-13%</td>
<td>1061</td>
<td>950</td>
<td>-10%</td>
</tr>
<tr>
<td>2</td>
<td>Dementia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>T.I.A.</td>
<td>37</td>
<td>40</td>
<td>41</td>
<td>83</td>
<td>82</td>
<td>79</td>
<td>57</td>
<td>-27%</td>
<td>809</td>
<td>903</td>
<td>+12%</td>
</tr>
<tr>
<td>4</td>
<td>Bilateral C.V.D.</td>
<td>56</td>
<td>41</td>
<td>41</td>
<td>80</td>
<td>80</td>
<td>42.1</td>
<td>24.3</td>
<td>-42%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Dementia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td>Pseudodementia</td>
<td>51</td>
<td>38</td>
<td>40</td>
<td>84</td>
<td>80</td>
<td>29.5</td>
<td>24.7</td>
<td>-16%</td>
<td>457</td>
<td>441</td>
<td>-3.5%</td>
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<tr>
<td>7</td>
<td>Dementia</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Migraine</td>
<td>35</td>
<td>36</td>
<td>37</td>
<td>75</td>
<td>75</td>
<td>73.9</td>
<td>39.3</td>
<td>-46%</td>
<td></td>
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</tr>
<tr>
<td>9</td>
<td>T.I.A.</td>
<td>52</td>
<td>40</td>
<td>43</td>
<td>100</td>
<td>100</td>
<td>24.2</td>
<td>24.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Glioma</td>
<td>61</td>
<td>42</td>
<td>48</td>
<td>90</td>
<td>80</td>
<td>46.6</td>
<td>27.8*</td>
<td>-38%</td>
<td>411</td>
<td>409</td>
<td>-3.5%</td>
</tr>
<tr>
<td>11</td>
<td>T.I.A.</td>
<td>54</td>
<td>39</td>
<td>39</td>
<td>100</td>
<td>100</td>
<td>24</td>
<td>25</td>
<td>-9%</td>
<td>590</td>
<td>789</td>
<td>+34%</td>
</tr>
</tbody>
</table>

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*Corrected value for PaCO₂ change; †p <0.001; ‡not significant.
fall unless the brain continues to be activated in some way. Therefore the first CBF measurement may not provide an appropriate base-line against which to measure the effect on CBF of stimuli administered after an interval. As the difference between two measurements of CBF at a 30 minute interval in an unstimulated patient may be as much as 40%, it cannot be dismissed as insignificant. Failure to appreciate that the first measurement is of CBF in an "activated" brain and not a basal value will lead to underestimation of the increase of CBF caused by subsequent mental activity.

Likewise the increase of CBF caused by a vasodilator drug will be grossly underestimated, particularly in human studies. However, even animal studies in the early assessment of such drugs, use an anesthetic regime similar to the one described above on the assumption that reasonably constant baseline CBF values will be obtained. Though the difference between two measurements of CBF at a 30 minute interval in an unstimulated patient may be as much as 40%, it cannot be dismissed as insignificant. Failure to appreciate that the first measurement is of CBF in an "activated" brain and not a basal value will lead to underestimation of the increase of CBF caused by subsequent mental activity.

Sequential studies are advisable before assumptions of a steady-state are made. The base-line measurement of CBF will fall unless the brain continues to be activated in some way. Therefore the first CBF measurement may not provide an appropriate base-line against which to measure the effect on CBF of stimuli administered after an interval. As the difference between two measurements of CBF at a 30 minute interval in an unstimulated patient may be as much as 40%, it cannot be dismissed as insignificant. Failure to appreciate that the first measurement is of CBF in an "activated" brain and not a basal value will lead to underestimation of the increase of CBF caused by subsequent mental activity.

Likewise the increase of CBF caused by a vasodilator drug will be grossly underestimated, particularly in human studies. However, even animal studies in the early assessment of such drugs, use an anesthetic regime similar to the one described above on the assumption that reasonably constant baseline CBF values will be obtained. Though the anesthetic itself may not affect CBF, it is clear that the lapse of time will and CBF will fall as the brain becomes less alert. Sequential studies are advisable before assumptions of a steady-state are made. The base-line measurement of CBF should be made only after the brain has become accustomed to the experimental situation. If it is necessary to make the first measurement of CBF before the brain is "at rest," then continued activation must be maintained during subsequent measurements.

Acknowledgments

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References

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N I Palmer, D J Thomas, B B MacGillivray, G H Du Boulay, J Marshall, R R Russell and L Symon

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