Cerebral Oxygen Extraction, Oxygen Consumption, and Regional Cerebral Blood Flow During the Aura Phase of Migraine

Lars Friberg, MD; Jes Olesen, MD, PhD; Niels A. Lassen, MD, PhD; Tom Skyhøj Olsen, MD, PhD; Agnete Karle, MD

Background and Purpose The aura phase of migraine is associated with focal blood flow changes, but it has been largely unknown whether these changes are correlated to changes in the cerebral metabolism.

Methods Eight patients required carotid angiography for evaluation of transient neurological attacks. Cerebral blood flow (CBF) results, angiography, and clinical observations subsequently suggested the diagnosis: migraine with aura and occasional aura attacks without headache. In the same setting the cerebral angiography was followed by four to six repeated recordings of regional CBF using the intra-arterial 133Xe injection method. Blood samples were drawn from the carotid artery and the internal jugular vein to measure oxygen extraction fraction and cerebral metabolic rate for oxygen.

Results The intracarotid regional CBF technique provoked aura symptoms and typical, migraine-related, posterior focal hypoperfusion in four patients, followed by typical unilateral headache in three patients. The remaining four patients had no symptoms or regional CBF changes during the examination. There was a significant increase (mean, 13%) of global oxygen extraction fraction in the four patients during aura symptoms, whereas no significant changes of oxygen extraction fraction were found in the nonsymptomatic group. The increase in global oxygen extraction fraction in the symptomatic group coincided with a drop in hemispheric CBF (mean 11%). Cerebral metabolic oxygen rate remained essentially unchanged, as did Paco2.

Conclusions The data presented suggest that the focal flow reduction during the migraine-aura phase is not a secondary phenomenon of reduced cerebral metabolism. However, arteriolar vasoconstriction might offer a possible explanation for the regional CBF changes observed during the migraine aura.

Key Words • metabolism • migraine • oxygen • cerebral blood flow

During migraine attacks with aura, a focal reduction of regional cerebral blood flow (rCBF) has been reported, usually in the posterior aspect of one hemisphere.1-3 It is still debated whether this flow reduction is secondary to reduced cortical neuronal activity or it reflects a primary vasoconstriction.4 Such vasoconstriction would have to be on the level of the resistance vessels (mainly arterioles), as angiographically significant hemodynamic spasms of the large arteries have been seen only in exceptional cases during migraine attacks.5 Positron emission tomography would be the examination method of choice to study metabolic changes, but to our knowledge only one study of regional oxygen metabolism during migraine attacks in three patients has been performed.6 Of these patients, only one was studied during the aura phase. In this patient there was increased oxygen extraction in the posterior aspect of the brain where rCBF was also reduced. A primary reduction in neuronal activity lowers the metabolic demand and CBF proportionally, and oxygen extraction remains largely unaltered.7 In this study we measured the arteriogenous oxygen differences over the brain during migraine attacks with aura simultaneously with serial recordings of rCBF.

Materials and Methods

This investigation comprised eight patients, five women and three men (mean age, 40.4 years; range, 30 to 53 years) (Table 1). The patients suffered from attacks that could be classified as migraine with typical aura (classification code 1.2.1) or aura attacks without headache (classification code 1.2.5).8 Before this investigation they all had experienced both types of attacks. They were submitted for cerebral angiography and rCBF examination because their neurological symptoms could not rule out that the cause of their attacks could be transient ischemic cerebral episodes. Excluded were patients in whom the angiography revealed signs of intracranial or extracranial arteriosclerosis. The protocol was approved by the Ethical Committee for Copenhagen and Frederiksberg Counties. All patients consented to participate in the scientific part of the investigation (jugular vein catheterization and collection of blood samples) after having received written and oral information. In conjunction with blood samples drawn for measurement of oxygen metabolism, we obtained blood samples analyzed for vasoactive neuropeptides from the same patient group. Results from that part of the investigation will be reported elsewhere. Information about patients is given in Table 1.

Puncture of the relevant common carotid artery was done using local anesthesia, and angiography of the carotid system and cerebral vessels was performed by administering the contrast medium through the cannula. The angiograms were

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inspected immediately. Using the Seldinger technique, we introduced a small, soft polyethylene catheter into the internal carotid artery after the angiography. In three patients (Nos. 3, 4, and 5), it was not technically possible to introduce the catheter into the internal carotid artery; therefore, the tip of the catheter was placed in the common carotid artery 1 to 2 cm below the bifurcation. These three patients did not develop aura symptoms or migraine headache in connection with the examination (Table 1). From the angiograms it was decided which of the two internal jugular veins had the largest diameter and therefore drained the largest portion of blood from the brain. Generally, one jugular vein was considerably larger than the other. After a direct puncture using local anesthesia, the largest vein was catheterized by Seldinger technique, and the catheter was advanced proximally placing the tip of the catheter a few centimeters from the bulbus. Thus, the intracarotid and jugular vein catheters were not necessarily placed on the same side of the neck. Five to six sets of blood samples were taken simultaneously from the two catheters. The arterial sample was obtained by mounting a low-friction glass syringe on the catheter, allowing the syringe to be filled by the suction of the syringe. Each blood sample was analyzed twice, and the mean concentrations were analyzed on the routine autoanalyzer in the Department of Clinical Chemistry. Oxygen extraction fraction (OEF) was calculated in percent as OEF equals arterial oxygen content at 100% saturation (1.34 mL O₂/g), and CBF is the cortical mean flow (mL/100 g/min).

We have chosen to define a hypoperfused region as 10 neighboring detectors each having a rCBF value at least 20% lower than that found during measurement when there were no symptoms and the rCBF pattern was evaluated to be normal. The collecting syringes were immediately stored on ice and transferred to the analyzer. Oxygen and carbon dioxide content was analyzed using an ABL (III) autoanalyzer (Radiometer). Each blood sample was analyzed twice, and the mean value was used for further calculations. Hemoglobin concentrations were analyzed on the routine autoanalyzer in the Department of Clinical Chemistry. Oxygen extraction fraction (OEF) was calculated in percent as OEF equals arterial oxygen saturation minus venous oxygen saturation. Cerebral metabolic rate for oxygen (CMRO₂) was calculated as

\[ CMRO₂ = Hb \cdot wHb \cdot O₂Hb \cdot OEF \cdot CBF \] (mL O₂/100 g/min)

where Hb is the hemoglobin concentration (mmol/mL), wHb is the relative weight of hemoglobin (16.125 g/mol), O₂Hb is the relative oxygen content at 100% saturation (1.34 mL O₂/g), and CBF is the cortical mean flow (mL/100 g/min).

We chose to perform statistical analysis on calculated percent-change data after plotting both absolute-change and percent-change data versus baseline values and ensuring that the percent changes were independent of the baseline values. The first set of blood obtained for each patient (time, 0 minutes) was used as a baseline value. The statistical analysis was carried out on serial measurements from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient. We analyzed the data for significant changes in the area under the curve (AUC) and maximum values on data from each patient.
patients did not develop neurological symptoms or developed aura symptoms (Figure). In three of these patients, this coincided with development of the typical focal hypoperfusion that has been described extensively in previous publications from our group using the same rCBF method as in this study.\textsuperscript{2,3,6} rCBF in the hypoperfused region dropped between 20% and 30%. The hypoperfused region included most of the occipital lobe and the posterior aspect of the parietal and temporal lobes of the affected hemisphere. In the remaining part of the affected hemisphere, rCBF was essentially unaffected throughout the examination. There were no systematic changes in Paco\textsubscript{2}; specifically, the Paco\textsubscript{2} changes could not account for the changes in global CBF. (See Table 1 for corresponding values of Paco\textsubscript{2} and global CBF.)

When rCBF was measured at the time the patients were experiencing symptoms, the number of detectors recording rCBF values ≤20% below mean hemispheric CBF was a minimum of 32 to 43, increasing to a maximum of 68 to 94 detectors during subsequent rCBF recordings. Each detector covered 0.9 cm×0.9 cm=0.81 cm\textsuperscript{2} of the outer brain surface. This corresponded to a minimum of 26 to 35 cm\textsuperscript{2} (13% to 17%) and a maximum of 55 to 76 cm\textsuperscript{2} (27% to 37%) of the outer surface of the hemisphere.

In the four nonsymptomatic patients the rCBF distribution was normal and unchanged throughout the examination. A computed tomographic scan of patient No. 3 revealed an infarct in the left occipital lobe; correspondingly, the patient had right-sided homonymous hemianopsia, which had developed in connection with a migrainelike attack a few weeks before our examination. This patient did not develop symptoms during the present examination, and the rCBF pattern was normal. The infarct was localized in the posterior cerebral artery domain, which explains why it was not visualized by the rCBF recording during which the flow tracer was administered only to the anterior and middle cerebral artery supply territories of the examined hemisphere.

As shown in the Figure, there was a significant, systematic increase in oxygen extraction in the patients who developed a migraine attack compared with those who had no symptoms, while the OEF changes in the nonsymptomatic patients were less marked and not significant (Table 4).

The mean value of maximum OEF increase was 8.3% higher (P<.0001) in the attack group than in the nonsymptomatic group (Table 4). CMRO\textsubscript{2} was essentially unchanged. It could be ruled out that the systematic global CBF decreases were caused by corresponding decreases in Paco\textsubscript{2}. We have given the measured Paco\textsubscript{2} values in Tables 2 and 3. However, in this study we have not corrected the individual CBF values for changes in Paco\textsubscript{2} because the cerebrovascular CO\textsubscript{2} response most likely is abnormal in the region affected by hypoperfusion during migraine aura.\textsuperscript{3,20,21}

### Discussion

The present study contains important information about changes in oxygen metabolism in the human brain during the onset phase of migraine aura. Taking into consideration the typical blood flow results, the normal angiography, other laboratory investigations, and the cerebral imaging and the subsequent course of the patients, we can conclude that these patients in fact had migraine with aura. The investigation provided a unique
TABLE 2. Measured and Calculated Values for Four Patients Having Migraine Attack With Aura

<table>
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<tr>
<th>Patient No.</th>
<th>Symptoms*</th>
<th>CBF Time, min</th>
<th>Global OEF, %*</th>
<th>Global CMRO₂, ml/100g/mln</th>
<th>PCO₂, mm Hgt</th>
<th>Global CBF, ml/100 g/mlnt</th>
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CBF indicates cerebral blood flow; OEF, oxygen extraction fraction; CMRO₂, cerebral metabolic rate for oxygen; and (Aura), aura in regression.

*Symptoms present during regional CBF measurement
**Calculated values.

opportunity to record the changes from the very beginning of the attack, as the attack was triggered by the investigation procedure (most likely the cerebral angiography). The study showed that the global cerebral oxygen extraction increased during the aura phase of a migraine attack simultaneously with the development of focal hypoperfusion. CMRO₂ was largely unaffected, and the CBF decrease was of the same magnitude as the OEF increase. Because the CMRO₂ in brain tissue was unchanged during the aura phase, it became clear that the CBF reduction was not a phenomenon secondary to reduced oxygen metabolism.

In the one patient studied with positron emission tomography during migraine aura, the findings were focally reduced CBF, focal increased OEF, and normal focal oxygen consumption.9 Our results are in full agreement with this.

The intra-arterial procedure often triggers an attack in patients suffering from migraine with aura. Sometimes the attack starts during the angiography but more often begins up to 1 hour after.1,6,7,10,15 In this study three patients had the tip of the arterial catheter placed in the common carotid artery, not in the internal carotid artery as did the remaining five patients. However, the oxygen content in the common carotid artery did not differ from that in the internal carotid artery. It is our clinical experience that attacks are more likely to precipitate when the tip of the catheter is placed in the internal carotid artery. For the purpose of measuring arteriovenous differences of oxygen content over the brain, we do think that the material can be considered homogeneous. The four patients who did not develop attacks served as control subjects.

Because of the two-dimensional nature of the detector system, the 133 Xe clearance from both submerged and superficial cortical tissue is recorded as projected to the outer, spherical hemispheric surface. This is two to three times smaller than the actual surface of the folded cortical structure, and this study did not provide information on the exact anatomy of the cortical structures below the spherical surface. Second, we have only an outline of the rCBF distribution for four to six 1-minute glimpses during the whole 30- to 40-minute period over which the rCBF changes evolved. For these reasons the largest area of the cortical surface affected by hypoperfusion can only be estimated to between 20% and 40% of the total hemisphere.

Theoretically, rCBF values recorded by a common carotid artery injection tend to be lower than those after intracarotid injection because they are influenced by the slow washout of isotope distributed to extracranial structures. However, because more than 80% of the common carotid blood flow enters the internal carotid artery, the extracranial contribution to the total measured radioactivity is small. Usually, extracranial blood flow is low and approximates the levels of white matter flow.22 In this study we used the initial slope as an expression for the cortical (gray matter) rCBF; this
value greatly favors detection of high rCBF values (cortical). Therefore, the errors of the calculated rCBF values obtained in the three patients undergoing common carotid $^{133}$Xe injections are minor (underestimated less than 5%) and cannot be considered of major importance in relation to the calculations of CMRO$_2$.

The precise level of reduced tissue perfusion in the affected focus of the brain might not be measured correctly with the intra-arterial $^{133}$Xe injection technique. This might be partly due to some influence of scattered radiation, which tends to smooth out differences between rCBF in the hypoperfused region and normal blood flow values in the remaining normally perfused brain regions. Furthermore, there are observations indicating that tissue perfusion is not constant over time in the affected focus and that the obtained rCBF values only represent mean values over the recording time. Actually, rCBF might drop to very low

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**Table 3. Measured and Calculated Values for Four Patients Without Symptoms**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>CBF Time, min</th>
<th>Global OEF, %*</th>
<th>Global CMRO$_2$, mL/100 g/min†</th>
<th>Pco$_2$, mm Hg*</th>
<th>Global CBF, mL/100 g/min*</th>
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CBF indicates cerebral blood flow; OEF, oxygen extraction fraction; and CMRO$_2$, cerebral metabolic rate for oxygen.

*Measured values.
†Calculated values.

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**Table 4. Statistical Analysis of Serial Data**

<table>
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<th>Attack Mean (range), n=4</th>
<th>No Attack Mean (range), n=4</th>
<th>Difference of Means</th>
<th>95% Confidence Intervals*</th>
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<td>Global OEF, AUC/min</td>
<td>4.28 (2.9 to 4.50)</td>
<td>1.85 (0.28 to 4.45)</td>
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<td>Global CMRO$_2$, AUC/min</td>
<td>–0.70 (–6.73 to –0.68)</td>
<td>2.39 (–0.65 to 4.30)</td>
<td>3.09</td>
<td>–8.92 to 2.74</td>
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<td>Global CBF, AUC/min</td>
<td>–4.71 (–8.74 to –0.43)</td>
<td>–0.22 (–4.81 to 3.24)</td>
<td>–4.55</td>
<td>–9.55 to 0.58</td>
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<td>Global OEF, maximum values</td>
<td>13.1 (11.7 to 15.1)</td>
<td>5.3 (3.4 to 6.2)</td>
<td>7.8</td>
<td>5.64 to 9.87†</td>
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<tr>
<td>Global CMRO$_2$, maximum values</td>
<td>6.26 (–3.10 to 21.47)</td>
<td>8.68 (5.50 to 13.56)</td>
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<td>–14.51 to 9.67</td>
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<tr>
<td>Global CBF, maximum values</td>
<td>–0.19 (–4.08 to 0.00)</td>
<td>2.59 (–9.67 to 11.26)</td>
<td>2.78</td>
<td>–13.76 to 8.21</td>
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OEF indicates oxygen extraction fraction; CMRO$_2$, cerebral metabolic rate for oxygen; AUC, area under the curve; and CBF, cerebral blood flow.

*Calculated by two unpaired samples.
†P<.001.
global OEF changes observed during attack reflected 
ing that true rCBF in this focus approached lower values 
increased focal OEF in the hypoperfused focus, indicat-
erg, local CMRO₂ is either normal or exhibits only 
changes in the majority of aura attacks affect only one 
moderate changes that could not be picked up with the 
sured as a global value.

During attack. This suggests that the rCBF reduction 
affected 10% to 20% of the total brain because the rCBF 
changes in the majority of aura attacks affect only one 
hemisphere.²⁵ A weighted estimate of the actual regional 
OEF changes within the hypoperfused region would result 
in a much higher regional OEF than that actually mea-
sured as a global value.

The possible conclusions from this study are: (1) Most 
importantly, hemispheric CMRO₂ is unchanged during 
the early phase of attacks of migraine with aura. There-
fore, local CMRO₂ is either normal or exhibits only 
moderate changes that could not be picked up with the 
current method. (2) Marked focal reduction of rCBF 
during attacks of migraine with aura is due to vasocon-
striction and is not secondary to decreased metabolism. 
(3) One interpretation of the data could be that the 
global OEF changes observed during attack reflected 
increased focal OEF in the hypoperfused focus, indicat-
ing that true rCBF in this focus approached lower values 
than were actually measured with the **Xe clearance technique.

References

1. Sldnhøj E, Paulson OB. Regional cerebral blood flow in internal 
569-570.

2. Olesen J, Larsen B, Lauritzen M. Focal hyperemia followed by 
spreading oligemia and impaired activation of rCBF in classic 

3. Lauritzen M, Skyhøj Olsen T, Lavsen NA, Paulson OB. Changes of 
regional cerebral blood flow during the course of classic migraine 

4. Lauritzen M, Larsen J. Regional cerebral blood flow during migraine 
attacks by Xenon-133 inhalation and emission tomography. Brain. 

5. Friberg L. Cerebral blood flow changes in migraine: methods, 

scintillation camera with 254 channels. J Nucl Med. 1977;18: 
168-174.

7. Lavsen NA, Roland PE, Larsen B, Melamed E, Sok H. Mapping of 
the human cerebral function: A study of the regional cerebral blood 
flow pattern during rest, its reproducibility and the activations seen during 
both sensory and motor functions. In: Lavsen NA, Ingvard DH, eds. 
Cerebral Function, Metabolism and Circulation. Copenhagen, 
Denmark: Munksgaard; 1985:127-130.

8. Headache Classification Committee of the International Headache 
Society. Classification and diagnostic criteria for headache dis-
orders, cranial neuralgias and facial pain. Cephalalgia. 1988; 
8(suppl 7):1-161.

9. Olesen J, Paulson OB, Lavsen NA. Regional cerebral blood flow in 
man determined by initial slope of the clearance of intra-arterially 

10. Herold S, Gibbs JM, Jones APK, Brooks DJ, Frakowiak RSJ, Legg 
1985;Suppl I, A45-46.

11. Widén L. How shall we measure regional brain work? In: Lavsen NA, 
Ingvard DH, Rahrle ME, Friberg L, eds. Brain Work and Mental 
Activity: Quantitative Studies With Radioactive Tracers. Copenhagen, 
Denmark: Munksgaard; 1986;220-235.

scintillation camera with 254 channels. J Nucl Med. 1977;18: 
168-174.

13. Gardiner JM, Allman DG, Campbell MJ, Royston P. Analysis of 
serial measurements in medical research. Br Med J. 1990;300: 
230-235.

14. Hansson L. A refinement to the analysis of serial data using 

15. Kaiser L. Adjusting for baseline: change or percentage change? 

16. Mathews JNS, Allman DG, Campbell MJ, Royston P. Analysis of 
serial measurements in medical research. Br Med J. 1990;300: 
230-235.

17. Mathews JNS. A refinement to the analysis of serial data using 

scintillation camera with 254 channels. J Nucl Med. 1977;18: 
168-174.

19. Olesen J, Paulson OB, Lavsen NA. Regional cerebral blood flow in 
man determined by initial slope of the clearance of intra-arterially 

flow changes in migraine: methods, observations and hypothesis. J 

21. Skyhøj Olsen T, Friberg L, Lavsen NA. Ischemia may be the 
primary cause of the neurological deficits in classic migraine. Arch 
Neurol. 1987;44:156-161.

22. Janzen R, Tanzer A, Zschocke S, Dieckmann H. Postangiogra-
phische SpStreaktionen der Hirngefasse bei Migranie-Kranken. Z 
Neurol. 1972;201:24-42.

23. Rahrle ME, Widén L, Friberg L, et al. Cerebral blood flow changes in 

24. Friberg L. Cerebral blood flow changes in migraine: methods, 

25. Friberg L. Cerebral blood flow changes in migraine: methods, 
Cerebral oxygen extraction, oxygen consumption, and regional cerebral blood flow during the aura phase of migraine.

L Friberg, J Olesen, N A Lassen, T S Olsen and A Karle

Stroke. 1994;25:974-979
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