Monitoring CBF in Clinical Routine by Dynamic Single Photon Emission Tomography (SPECT) of Inhaled Xenon-133

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SUMMARY A very simple and low-cost brain dedicated, rapidly rotating Single Photon Emission Tomograph SPECT is described. Its use in following patients with ischemic stroke is illustrated by two middle cerebral artery occlusion cases, one with persistent occlusion and low CBF in MCA territory, and one with early lysis of the occlusion having high CBF (massive luxury perfusion) for some weeks. Evidence of this kind may be essential in the evaluation of therapeutic measures in ischemic stroke.

Stroke Vol 17, No 6, 1986

MANY STROKE PATIENTS with seizable ischemic infarction on CT scans and with severe neurological deficits have no arterial occlusions on angiography studied on admission in the acute state. Such patients typically have focal hyperemia of the infarct area instead of focal ischemia when studied soon after admission: when studied within 4 days of stroke onset about one third of patients with extensive infarction in the MCA territory have hyperemia in the infarct area due to spontaneous lysis of an embolic MCA occlusion.

This dynamic event, the hyperemic period, may be monitored by sequential studies of cerebral blood flow CBF as illustrated in this article reporting two cases of MCA occlusion and ischemic infarction on CT scan, one with persistent low flow and one with massive but transient hyperemia. The data were obtained by a simple tomographic device for imaging CBF by Xenon-133 inhalation. It is postulated, that any causal therapeutic intervention in the phase of ischemic stroke must take into account whether or not focal ischemia is still present or it has already spontaneously been replaced by hyperemia.

Method

rCBF was measured tomographically in a single plane situated 5 cm above the orbito-meatal plane by using a dynamic single photon emission tomograph (D-SPECT) with a detector system containing 32 sodium-iodide crystals (TOMOMATIC-32; Mediamatic Ltd. Denmark). $^{133}$Xe-gas was administrated by rebreathing through a mouthpiece for 1.5 minutes. During this period and for the following three minutes of $^{133}$Xe wash-out, a series of 4 consecutive $^{133}$Xe distribution maps of the brain was taken, the data collection periods being one-and-a-half minute for the first period and one minute for three subsequent ones. Approximately 60 to 80 mCi of $^{133}$Xe gas was admixed to a 4 liter rubber bag containing atmospheric air. This results in a counting rate of approximately 200,000 counts per minute in the second one-minute period of the highest counting rate.

The spatial resolution (FWHM) in this equipment, as assessed by phantom studies using $^{133}$Xe, is approximately 20 mm axially as well as transversely. It varies a little depending on the distance from the detector system (poorest resolution in the center of the image). The energy discrimination level was adjusted to 20% below the photopeak of 81 keV.

rCBF values were calculated from the 4 consecutive $^{133}$Xe tomograms by using the algorithm of Celsis et al "early picture method" and "sequence of pictures method". In this calculation a selection must be made of the cut-off point of high count rate pixels taken to represent grey matter dominated pixels. We used a cut-off point at 70% of the maximal counting rate.

The results were displayed as rCBF tomogram in a 128 $\times$ 128 matrix with a 16 level color-scale. They are also extracted as absolute values as a print-out of the data in a 32 $\times$ 32 matrix with each pixel corresponding to an area of approximately 7 mm $\times$ 7 mm. In this print-out each hemisphere comprised 150 to 190 pixels depending on the size of the head.

A blood:brain partition coefficient of 0.85 ml/g was used for calculating the absolute flow levels from the high count rate pixels assumed to represent mainly grey matter regions. Thus calculated, the normal hemispheric CBF values were 58.2 $\pm$ 8.3 ml/100 g/min (n = 11, age 40.4 $\pm$ 11.8 years, ApCO$_2$ = 42.8 $\pm$ 5.7 mm Hg, MABP = 105 $\pm$ 17 mm Hg). No significant right-to-left hemispheric asymmetry was observed as the average difference between right and left side expressed in percent was 1.1 $\pm$ 0.8% (mean value $\pm$ standard error of mean value, n = 11).

Case Stories and Results

Case 1, Ischemic Infarct

A fifty-eight year old man, previously healthy, was admitted after sudden onset of right-sided hemiplegia and severe global aphasia. He showed some degree of recovery, was able to walk with a cane 2 months later despite persisting paralysis of the arm. The aphasia had only recovered partially. CT-scan showed a large low density area in the left MCA territory (fig. 1, f). Carot-
id angiography on the 3rd day after onset revealed left-sided MCA stem occlusion. Persistent occlusion of the same site was verified by digital subtraction angiography on the 44th day.

CBF was measured on days 2, 10, 13, 38, and 52 (fig. 1 a-e). In the infarct area CBF remained low throughout the recording period although a transient period with a moderate rise in this low flow was observed.

Case 2, Hyperemic Infarct

A sixty year old man with past history of myocardial infarction was admitted with sudden onset of right-sided moderate hemiparesis and severe global aphasia. The hemiparesis recovered almost completely within 2 weeks, but the aphasia showed only moderate improvement. CT-scan showed a large low density area in the left MCA (fig. 2 f). No occlusions were seen on angiography, neither in the internal carotid artery nor in the MCA territory. A rapid transit of the contrast medium from arterial to venous phase (early filling veins) was noted angiographically on the 2nd day. The results point to a transient occlusion of the MCA stem by an embolus followed by subsequent complete recanalization.

CBF was measured on days 8, 10, 15, 22, and 43 (fig. 2, a-e). Blood flow in the affected (left) MCA territory was initially markedly increased above the normal level (black area in the CBF tomogram means high flow values beyond color-scale). The calculated mean CBF values of the whole affected MCA territory was 119, 87, 55, 34, and 31 ml/100 g/min for the five studies respectively. Hence the hyperemic state persisted for about two weeks. After some weeks, the same low CBF as in the patient with permanent MCA occlusion was attained.

Discussion

Because Xenon-133 is used as tracer, CBF in the low flow areas will be somewhat overestimated. The method is, therefore, not suitable for quantitative assessment of flow in focal low flow areas. However, the method is able to demonstrate qualitative inter- and intra-individual changes of flow during the time course of the post-stroke period. Repeated CBF measurements by SPECT allow the demonstration non-in-

FIGURE 1. rCBF tomogram in case 1 (left MCA stem occlusion) at the resting state in the various periods after onset (a, b, c, d, e) and plain CT scan (f). rCBF tomograms are expressed in the same color-scale (ml/100 g/min). Arrows on figures b and c indicate the area of transient relative hyperemia on days 10 and 13.
FIGURE 2. rCBF tomograms in case 2 (recanalization of left MCA stem occlusion) at the resting state in the various periods after onset (a, b, c, d, e) and plain CT scan (f). rCBF tomograms are expressed in the same color-scale (ml/100 g/min).

vasively and at fairly low cost of the time course of CBF changes in the post-stroke period.

The Hyperemic Infarct

In the MCA territory of the ipsilateral hemisphere of case 2, we observed a widespread and dramatic CBF increase reaching values much higher than in normal man. This high flow is undoubtedly much in excess of the necrotizing tissue's metabolic demand. This observation is based on positron emission (PET) studies that never have shown a stroke case with high oxygen uptake of the infarct. Such hyperemia was first described as "luxury-perfusion" by Lassen, and subsequently many others have reported the same phenomenon, showing that it is a rather frequent phenomenon of transient nature (lasting a few weeks) in acute infarction. It is noteworthy that the luxury-perfused hemisphere finally attained the same low CBF as in the patient with permanent MCA occlusion. This final stage was reached about 6 to 8 weeks after the acute onset (fig 2, 2-e).

The Ischemic Infarct

In case 1, CBF remained lowest on the diseased side. However, a moderate and transitory CBF increase was revealed by the sequential studies. This suggests that two different phases had occurred one after the other before this occluded hemisphere finally reached its final state of very low flow, presumably matching a very low rate of oxidative metabolism: the severe CBF reduction on the 2nd day after onset may, as reported by Wise et al, represent a situation of increase of the oxygen extraction rate (OER) compensating for the reduced CBF (so-called "misery-perfusion"). The transient CBF increase observed on the 10th and 13th day (fig. 2-b, c: arrow), in all probability, represents a state of relative hyperemia. It is in this phase that PET studies consistently show luxury-perfusion as evidenced by a decreased focal OER. The temporary CBF increase could be explained by some degree of partial restoration of the local perfusion pressure combined with persistent vasoparalysis. This restoration is not due to thrombolysis as reangiography showed persistent occlusion on day 44. It is more likely that it is caused by hypertrophy of collateral channels. The phase of relative hyperemia implies that the normal regulation of CBF in accordance with local metabolic needs has not yet been regained in the infarcted area at this period of 2 to 3 weeks after onset, and case 1 is therefore in this respect similar to case 2.
Formation of new capillaries in the process of absorption of necrotic tissue (i.e. granulation tissue) may also contribute to this transient increase of flow. This process reaches its maximum during the 2–4 weeks after the stroke and is completed after about 6 weeks.  

Comment

These data demonstrate the feasibility of monitoring CBF repeatedly in ischemic stroke documenting the consequence of spontaneous desobliteration by a fairly simple technique. It should be stressed that ischemic CUD due to occlusion of a major artery typically results in flow alterations in sizeable brain areas. Thus, the limited spatial resolution obtained with the instrumentation used is not a major problem. The observations are considered essential for classifying patients subjected to therapeutic interventions (e.g. hemodilution) aimed at relieving ischemia: it would, a priori, seem essential to know if extensive focal ischemia is still present or not.

References

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H Sugiyama, J Christensen, T Skyhøj Olsen and N A Lassen

Stroke. 1986;17:1179-1182
doi: 10.1161/01.STR.17.6.1179

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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