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O'Brien M D. Cerebral blood changes in migraine. *Headache* 10:139-43, 1971.

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Cerebral blood flow measurements were made in 7 patients during the prodrome of a migraine attack and in 10 patients during the headache stage. All patients were subsequently studied when asymptomatic. The results indicate that the aura stage of migraine is associated with a considerable reduction in cerebral cortex perfusion rates, and this reduction is a general and not a focal phenomenon. The headache stage may be associated with a small increase in cortex perfusion rates that could be a reactive hyperaemia. [The *SCI*® and *SSC*® indicate that this paper has been cited in over 95 publications, making it one of the most-cited papers from this journal.]

Cerebral Blood Flow in Migraine

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September 13, 1989

I joined John Butterfield's Department of Medicine at Guy's Hospital soon after qualification. Attached to the Department of Medicine was a Medical Research Council Unit under Norman Veall, who had spent some years developing a noninvasive method of measuring cerebral blood flow (CBF) by the inhalation of xenon-133. The only methods of CBF measurement available at the time were the Kety-Schmidt technique and the intracarotid xenon injection method. The inhalation technique had just reached the stage at which it could be used on patients; nobody else in the world had it, and, indeed, most experts of the day thought it impossible. For a young researcher, it was a marvellous opportunity to make observations that had not been possible before. The method was atraumatic, it was repeatable so that serial observations could be made, and it gave simultaneous bilateral measurements.

In 1966 I was asked to give a paper at the First Migraine Symposium¹ on CBF in migraine. Though at the time there were no reports of any direct measurements, I was able to include details of the first two patients we had studied, both of whom showed a significant reduction in CBF in the early stages of an attack, and this was the first ever report of a direct measurement of the cerebral circulation in a migraine attack. A preliminary communication followed in *Lancet*,² and the completed study formed the basis for my doctorate thesis.³

It was suggested that I submit this work for the Harold Wolfe Lecture Award in 1970, which is organized by the American Association for the Study of Headache. They reserve the right to publish any submission in their journal *Headache*. Although I did not get the award, my paper was published.

For many years it remained the only study of CBF during either the prodrome or the headache stage of a spontaneous migraine attack. One of the reasons for this was the considerable logistic difficulties in getting a measurement during the aura. It is not surprising therefore that all my subjects were either doctors or worked in the hospital and were available for study at the first sign of a migraine attack. A more recent series was published in 1984⁴ using xenon inhalation and SPECT, and this confirmed our original findings.

Our observations showed for the first time that CBF is reduced in the prodrome/aura of a migraine attack and, more controversially, this was a generalized phenomenon, not a strictly focal event as had been assumed up to that time. More recent studies have shown quite marked regional variation in flow, as we originally predicted. We also showed that these low flows continued into the headache stage, showing that the headache was not due to cerebral vasodilatation and explaining the concurrence of headache with aura in some patients. We only demonstrated a small increase in flow in the headache stage, findings subsequently confirmed by some and refuted by others. We postulated that this could be a reactive hyperaemia, implying that all migraine attacks have a vasoconstrictive phase, even if this is not clinically evident—a view that is still a matter of dispute.

It was some years before the xenon inhalation CBF technique was generally accepted, but it has now become the most widely used method, largely due to the computer program developed by Walter Obrist. It was also some years before the results of our CBF measurements were accepted and some aspects remain controversial.

1. O'Brien M D & Veall N. Cerebral blood flow measurements. (Smith R, ed.) *Background to migraine*. London: Heinemann Medical Books, 1967. p. 11-4.

2. O'Brien M D. Cerebral-cortex-perfusion rates in migraine. *Lancet* 1:1036, 1967. (Cited 40 times.)

3. ———. *Cerebral cortex perfusion rates in migraine*. PhD dissertation, University of London, 1973.

4. Lauritzen M & Olesen J. Regional cerebral blood flow during migraine attacks by xenon-133 inhalation and emission tomography. *Brain* 107:447-61, 1984. (Cited 50 times.)