Migraines: Unmasking the Causes

Blood flow, nerve receptors and enkephalins all seem to be involved in causing migraines

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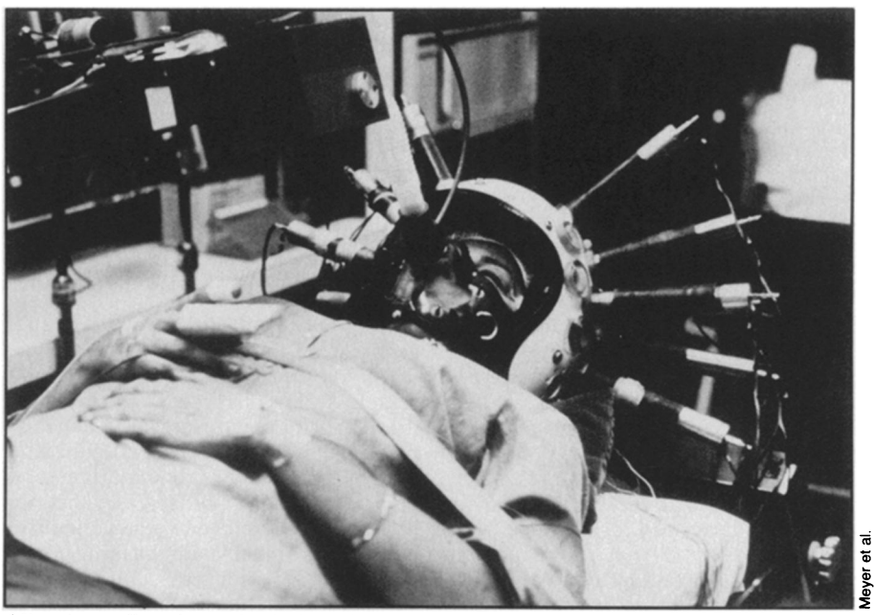

Meyer et al.

Migraine sufferer's cerebral blood flow monitored with the xenon technique.

For the 10 to 25 million persons who experience the blinding, often debilitating pain of a migraine, relief cannot come quickly enough. Researchers aware of their plight have been busy on many fronts trying to unlock the secrets of migraines. They gather yearly to present findings and compare notes. The past decade has been a particularly busy one for migraine researchers, and those at the 1980 annual meeting of the American Association for the Study of Headache in San Francisco presented findings that confirmed and extended earlier results: Blood flow, nerve receptors and enkephalins (pain-relieving chemicals in the brain) all play roles in the migraine problem.

During the late 1960s, M. D. O'Brien of Guy's Hospital in London and Eric Skinhøj and O. B. Paulson of Bispebjerg Hospital in Copenhagen pinpointed two major abnormalities that underlie migraine headaches — a decrease in the blood flow through the brain before the headache and an increase in the flow during the actual headache phase. The three researchers made the discovery in a handful of patients by using an invasive and therefore somewhat dangerous technique: They injected a needle into one of the two carotid arteries that run up the neck into the brain.

In the mid 1970s, Walter Obrist and colleagues at Duke University Medical Center in Durham, N.C., devised a noninvasive way to measure cerebral blood flow. A radioactively tagged gas, xenon, is breathed by a patient, and the speed at which xenon moves through the brain reflects the rate of cerebral blood flow.

John Stirling Meyer and colleagues at Baylor College of Medicine and the Veterans Administration Hospital in Houston then modified this technique to make it suitable for studying cerebral blood flow in headache patients. In their method, a patient puts on a motorcycle helmet with Geiger counters mounted in it and lies on a padded table to breathe mildly radioactive xenon through a face mask for one minute. The xenon goes from the lungs to the heart and then to the brain and is detected by the Geiger counters. The amount of time between the detection of the xenon by each of the Geiger counters is then recorded by a computer. If little time elapses between the detection at each counter, then the xenon is moving quickly, and blood is flowing quickly through that area of the brain; if xenon appears to move slowly, then so is the blood. The technique also allows the simultaneous measurement of blood flow through 16 different areas of both hemispheres of the brain, something that the carotid artery injection method did not do.

The next step Meyer and co-workers took was even more novel. They used their modified technique to undertake the first controlled clinical study to compare the cerebral blood flow of migraine patients before, during and after headache, and contrast it with that of other kinds of headache patients under comparable conditions, as well as with the cerebral blood flow of nonsufferers.

The results of this study, reported at the 1979 annual meeting of the AASH and winner of the 1979 Harold G. Wolff Award for outstanding research into the causes and treatment of headaches, confirm the findings of O'Brien, Skinhøj and Paulson concerning blood flow before and during migraine. But the findings included new discoveries as well. For instance, Meyer and co-workers found that when blood flow increases during migraine and cluster headache (similar to migraine in intensity but characterized by abrupt series or clusters of attacks), the increase is both inside the brain and in blood vessels leading to the scalp. In contrast to migraine and cluster headache sufferers, however, tension headache victims experience normal blood flow before, during and after headaches. In addition, they found that while both patients with migraines and those with cluster headaches have abnormal increases in blood flow for the duration of their headaches, this increase promptly subsides in cluster patients but tends to remain elevated in migraine patients for two to three days after the pain of a headache has subsided. Still another insight came from having subjects breathe five percent CO_2 (a known blood vessel dilator) mixed with air. The cerebral blood flow of those suffering from migraine overreacted to the dilator compared with that of healthy controls, often in those areas of their brains where the migraine patients suffered from headache. This finding implies a sensitivity of migraine patients' cerebral blood vessels to outside influences, such as circulating gases, chemicals or incoming nerve stimuli.

Meyer and his colleagues concluded that these abnormal and excessive blood vessel reactions might be steering them closer to the answer of why migraine victims have their devastating headaches in the first place. This conclusion, however, is not an original idea, Meyer is quick to point out: The pioneer headache researcher Harold G. Wolff postulated that cerebral blood vessels in migraine sufferers are excessively reactive.

Even more crucial, though, this confirmation of Wolff's hypothesis made Meyer and his colleagues wonder why the cerebral blood vessels of migraine patients are overly reactive to outside stimuli in the first place and why this usually involves one hemisphere of the brain. They wondered whether it might be because so-called sympathetic nerve alpha and beta

receptors on the vessels were abnormal. Such receptors, which control the expansion and contraction of cerebral blood vessels, are known not only to receive signals from incoming involuntary nerves but to be influenced by CO_2 and other chemicals in the blood.

Meyer and his team decided to test whether these receptors were responsible. They gave migraine patients drugs that are known to be both clinically useful for countering migraine pain and capable of stimulating alpha and beta nerve receptors on cerebral blood vessels. They then measured the patients' cerebral blood flow response to CO_2. Their results, reported at this year's AASH meeting, showed that this group of drugs tended to lessen the overreaction to CO_2 of the migraine patients. This finding, Meyer and his co-workers conclude, implies that the excessive responsiveness of migraine patients' cerebral blood vessels is due, at least in part, to abnormal alpha and beta receptors on the vessels.

In spite of these discoveries, the method by which abnormal cerebral blood flow leads to head pain during a migraine is not clear. It is possible that when cerebral blood vessels overreact to nerve messages or other chemical stimuli they first constrict quickly, subsequently expanding excessively. This could account for the initial cerebral blood flow decrease and the increased flow during the headache phase. Such an excessive expansion might impinge on pain-carrying nerves, which then send pain messages to pain centers in the brain.

What *is* now known for sure about migraine pain is that enkephalins become depleted at the beginning of the migraine attack but increase to normal levels as the headache subsides (SN: 6/21/80, p. 390). This finding, part of the research of Bruno Anselmi and co-workers at the University of Florence in Florence, Italy, was given the 1980 Harold G. Wolff Award at the AASH meeting and, along with the research of Meyer and colleagues, provides an indication that the researchers are on the right track: "What we found and what Anselmi found are complementary," Meyer told SCIENCE NEWS.

Taken all together these findings suggest that migraine sufferers have abnormal nerve receptors on cerebral blood vessels — abnormal receptors that allow the vessels to react excessively to gases, nerve messages or other stimuli and thereby bring about abnormal cerebral blood flow, usually a decrease, then an increase. The stretched vessels stimulate nerve fibers for pain. And thus when cerebral blood flow is increased, it results in pain stimulation that seems to cause, or at least be accompanied by, a depletion of brain pain-relieving chemicals. The results: excruciating head pain known as a migraine. □

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