CC/NUMBER 17
APRIL 23, 1984

This Week's Citation Classic

Harper A M, Deshmukh V D, Rowan J O & Jennett W B. The influence of sympathetic nervous activity on cerebral blood flow. *Arch. Neurol.* **27**:1-6, 1972.
[MRC Cerebral Circulation Res. Group, Wellcome Surgical Res. Inst., and Inst. Neurological Sciences, Univ. Glasgow, Scotland]

The effect on the cerebral blood flow (CBF) of stimulation of the cervical sympathetic trunk was explored in anaesthetised baboons at normocapnia and hypercapnia. Sympathetic stimulation produced a significant reduction in CBF during hypercapnia. It is argued that there is a dual control of CBF — the extraparenchymal vessels being influenced by sympathetic nerves while the intraparenchymal vessels are under local intrinsic metabolic regulation. The pial vessels are possibly influenced by both systems. [The *SCI*® indicates that this paper has been cited in over 175 publications since 1972]

A. Murray Harper
Wellcome Surgical Institute
University of Glasgow
Glasgow G61 1QH
Scotland

February 3, 1984

"After qualifying in medicine, I was awarded a research scholarship in the embryonic cardiovascular department at Glasgow Royal Infirmary in the late 1950s. At that time, it seemed a good idea to study the effects of cardiopulmonary bypass on the cerebral circulation. Before doing this, I had to set up techniques for measuring blood flow through the brain (in experimental animals) which avoided the artefact of 'extracranial contamination,' an artefact which bedevilled so many of the methods in use at that time. The effects of changing various physiological parameters on cerebral blood flow (CBF) had to be measured. Of particular importance were the blood gases, the arterial blood pressure, and their interrelationship. As far as I am aware, I was the first to demonstrate quantitatively the presence of cerebral 'autoregulation' — that is, the maintenance of a relatively constant CBF in the face of alterations in arterial blood pressure.[1] Interspersed with the development of methods which involved the first use of ^{133}xenon for the measurement of CBF in man[2] and other clinical studies, these 'control' studies (performed at the Wellcome Surgical Institute, University of Glasgow) took ten years.

"I was then convinced that the generally accepted view of the cerebral circulation— namely, that it was controlled by the metabolic needs of cerebral tissue —was correct, when a bombshell arrived. A paper published in 1969[3] suggested that extrinsic nerves (sympathetic and cholinergic) supplying the neck arteries and the carotid sinus played a major part in the control of cerebral circulation. My colleagues (a PhD student, V.D. Deshmukh; a physicist, J.O. Rowan; and a professor of neurosurgery, W.B. Jennett) and I decided that the observations were surprising on morphological grounds and, over several years, devised a series of experiments to test the effect of neurogenic influence on CBF.

"The paper is only one of a series, but I believe it is cited so frequently because it contains an important hypothesis —namely, that the sympathetic nerves in the neck can modulate the response of the cerebral blood vessels to changes in blood gases and blood pressure, but are not the ultimate controlling factor in the amount of blood perfusing any given area of the brain. It opened the way to the rational interpretation of the effects of carotid artery stenosis and ligation on CBF in animals and man which had considerable clinical benefits.[4] The paper also made one suggestion which led to a proliferation of studies throughout the world — namely, 'Sympathetic innervation may help to protect the intraparenchymal vessels during acute hypertensive episodes....' This was subsequently shown to be true.[5]

"Although I am still studying cerebral metabolism and blood flow, 26 years later I still have not got around to starting my original project!"

1. **Harper A M**. The inter-relationship between a PCO2 and blood pressure in the regulation of blood flow through the cerebral cortex. *Acta Neural. Scand.* 41(Suppl.14):94-103. 1965.
2. **Glass H I & Harper A M.** Measurement of regional blood flow in cerebral cortex of man through intact skull. *Briti Med. J.* **1**:593. 1963.
3. **James I M, Miller R A & Purves M J.** Observations on the extrinsic neural control of cerebral blood flow in the baboon. *Circ. Res.* **25**:77-93, 1969. (Cited 215 times.)
4. **Jennett B. Miller J D & Harper A M.** *Effect of carotid artery surgery on cerebral blood flow.* Amsterdam: Excerpta Medica. 1976. 170 p.
5. **Mackenzie E T, McGeorge A P, Graham D I, Fitch W, Edvinsson L & Harper A M**. Effects of increasing arterial pressure on cerebral blood flow in the baboon: influence of the sympathetic nervous system. *Pflügers Arch.—Eur. J. Physiol.* **378**:189-95. 1979.