The Control of the Cerebral Circulation

The history of concepts regarding the cerebral circulation has shown a somewhat circular course. Although dilatation of cerebral vessels in asphyxia had been noted as early as 1851, it was in 1890 that Roy and Sherrington developed the first generalizing concept regarding the physiologic regulation of cerebral blood flow. They recognized two important determining factors. The first of these was arterial blood pressure: "... the blood supply of the brain varies directly with the blood pressure in the systemic arteries. ... In whatever way produced, anemia of the central nervous system excites the vasoconstrictor nerves with the result that owing to constriction of the vessels of the digestive, urinary and other systems, the arterial blood pressure rises, causing an increased flow of blood through the cerebrospinal blood vessels." The second factor, although less obvious, was clearly defined as the intrinsic control of cerebral vessels. Although they found no evidence of intrinsic control by way of vasomotor nerves, they had observed during asphyxia or the intravenous infusion of acid an expansion of the brain independent of blood pressure, which they attributed to dilatation of its blood vessels. In a remarkably succinct insight they anticipated a half century of experimental progress in their interpretation: "that the chemical products of cerebral metabolism contained in the lymph which bathes the walls of the arterioles of the brain can cause variations of the calibre of the cerebral vessels: that in this re-action the brain possesses an intrinsic mechanism by which its vascular supply can be varied locally in correspondence with local variations of functional activity."

Six years later Leonard Hill published his book, The Physiology and Pathology of the Cerebral Circulation: An Experimental Research, which was to dominate the field for nearly two generations. Armed with a series of pressure measurements peculiarly unsuited to eliciting evidence for an intrinsic circulatory control of the brain, Hill found none, insisted therefore that none existed, and rebuked those who with more appropriate methods or sounder reasoning found evidence for its presence. "In every experimental condition the cerebral circulation passively follows the changes in the general arterial and venous pressures. ... The brain has no direct vasomotor mechanism, but its blood supply can be controlled indirectly by the vasomotor centre acting on the splanchnic area. The vasomotor centre is part of the central nervous system, and feels the same needs and is stimulated by the same centripetal impulses as affect the rest of that system, and thus it maintains a supply of blood to the central nervous system which..."
corresponds to its functional activity." It was Hill's concept that found its way into most of the textbooks of physiology for the first half of the twentieth century, while Roy and Sherrington's ideas were largely forgotten. Early in the 1930's and prompted by the work of Cobb,4 Forbes,4 Schmidt,5 and Wolff,6 there was a reawakening of interest in the intrinsic control of cerebral vessels, a questioning of Hill's dogmatic assertions, and a restatement of the dual control postulated by Roy and Sherrington. By 1950 it was possible to reinforce that concept by studies in man uncomplicated by anesthesia and surgical intervention: "Studies in intact human beings have strengthened the concept that a normal arterial blood pressure is zealously maintained by numerous homeostatic mechanisms such as the carotid sinus reflex and central control of peripheral vascular tone; and that as long as the mean arterial blood pressure remains above a critical minimal level, cerebral blood flow is actually regulated intrinsically by changes in cerebrovascular resistance."7

The supposition that this intrinsic control permits the adjustment of circulation locally to functional and metabolic demand has found considerable experimental reinforcement. Cobb and Talbott,8 Schmidt and Hendrix,8 and Serota and Gerard 10 have reported evidence for increased blood flow in those regions of the brain that have experienced an increase in functional activity. In our laboratory11 measurement of the circulation in some forty areas of the brain of animals in physiologic states has shown a remarkable correlation with presumed functional activity in the respective areas and with the distribution of cellular enzymes involved in oxidative metabolism. Photic stimulation, after a period of several minutes, results in a demonstrable augmentation of blood flow in the visual cortex, the lateral geniculate, and the superior colliculus.12

Furthermore, the thesis of Roy and Sherrington, that this response was effected by the vasodilator properties of the products of cerebral metabolism, finds support in the well-known ability of carbon dioxide to dilate cerebral vessels and decrease cerebrovascular resistance more profoundly than any other known substance.

In addition to humoral factors, the possibility of neurogenic influences in the intrinsic regulation of the cerebral circulation has been recognized for some time. Unmyelinated nerve fibers have been demonstrated on intracerebral blood vessels as has a vasoconstrictor control emanating from the cervical sympathetics and a vasodilator pathway in the greater superficial petrosal.4,13 It is one thing, however, to establish the existence of intracranial vascular nerves capable of constricting or dilating cerebral vessels, but quite another to demonstrate their physiologic function. Studies in man have failed to reveal a generalized tonic effect exerted by the cervical sympathetics on cerebral vascular tone14 except possibly in certain pathologic states,15 and the role of neurogenic influences on the normal cerebral vessels has remained obscure.

The review by Mchedlishvili, "Vascular Mechanisms Pertaining to the Intrinsic Regulation of the Cerebral Circulation," which appears elsewhere in this issue, is a welcome addition to the literature in this field. It describes studies in his laboratory and in those of his colleagues concerned especially with the neurogenic control of cerebral vessels other than the arterioles, which have received the bulk of attention elsewhere. It is not necessary to deny the importance of extrinsic factors to appreciate the role of the intrinsic control of the cerebral circulation. The recognition of neurogenic influences need not necessarily minimize the effects of carbon dioxide on cerebral vessels. Nor must one discard the theoretical calculations of Schleier16 and the direct evidence of Landis17 regarding the importance of arteriolar resistance in other vascular beds to accept the evidence of neurogenic influences on the larger vessels of the brain. Nevertheless, by calling our attention to an area of cerebral circulatory physiology that has been largely neglected and by making available to us a...
literature of which we are not always aware, the review by Mchedlishvili serves an important purpose in contributing to what will eventually be a better understanding of the control of the cerebral circulation.

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References


The Great Truth

Science seems to me to teach in the highest and strongest manner the great truth which is embodied in the Christian conception of entire surrender to the will of God. Sit down before fact as a little child, be prepared to give up every pre-conceived notion, follow humbly wherever and to whatsoever abysses Nature leads, or you shall learn nothing. I have only begun to learn content and peace of mind since I have resolved, at all risks, to do this.—Huxley.
Editorial: The Control of the Cerebral Circulation
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