Egas Moniz and cerebral angiography

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The author recalls many manifestations of Moniz's fertile mind, and in particular the story of his development of cerebral angiography. The Journal publishes this article in tribute to a great neuroscientist in this 100th year since his birth.

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It seems fitting at the time of the centenary of Egas Moniz's birth (November 27, 1874) to recount some aspects of a life so unusually fruitful in major contributions to medicine. In our generation dramatic advances in scientific knowledge rarely seem to emanate from solitary workers in poorly equipped or makeshift laboratories. The history of scientific and therapeutic progress in medicine reveals, however, that much has been accomplished in the past under these handicaps. Marston noted in a recent Cushing oration that "the evidence is clear that in medicine major innovations of significant impact and broad applicability have emerged as the result of the work of individuals and small groups pursuing ideas arising out of their own experience and reflecting their personal creativity."

Egas Moniz's major contributions to neurological sciences, cerebral angiography and prefrontal leukotomy, vividly illustrate this point.

Moniz was born in a small village in northern Portugal and received his medical education in the University of Coimbra. His career is unusual in that he did not begin his major investigations until the age of 51, a decade of life when many researchers are inclined to enlarge on their previous accomplishments. His scientific pursuits were delayed by a distinguished political career. He was Senator, Secretary for Foreign Affairs, and leader of the Portuguese delegation to the Peace Conference in 1918. Moniz felt that his political career gave him "some illusory success and many aggravations."

He considered himself a liberal and was a strong supporter of the political independency of academic institutions, and when he was Dean of the Medical School in Lisbon he spent a short period in prison after preventing the police from entering the campus during a student protest.

Disappointed by the turn of the political events, Moniz returned to his work as a neurologist. Influenced by the Pavlovian theories, he postulated that obsessive thoughts might be due to rigid neuronal connections. He was impressed by Bricker's description of the behavior of a patient upon whom Dandy has performed bilateral frontal lobectomies in exposing a meningioma. The man, a remarkable checker player, had much of his intellectual abilities preserved after the procedure. Interestingly
enough, Moniz makes only a brief comment on the significant experimental work on the frontal lobes being done by Fulton's group at Yale, and reported by Jacobsen to the Second Neurological Congress in London in 1935.\textsuperscript{13}

It is not the purpose of this essay, however, to discuss leukotomy, for which he was awarded the Nobel Prize in 1949, but rather to analyze the events which led to the introduction and expansion of angiography as a diagnostic tool.

Moniz did not become familiar with pioneer work of others in the field until late in his own investigations. He comments that much time and work might have been saved had he been aware of previous investigations.

Neurological diagnosis in Moniz's days was based on anatomical and pathological correlations, much of which had been established by the French school. Moniz trained with Pitres and regularly attended the clinics of Babinsky, Pierre Marie and Dejerine in Paris. It was in Paris that Moniz met Sicard, who, with Forestier, had introduced lipiodol myelography in 1921.\textsuperscript{28} The work of Dandy\textsuperscript{4} was well known in Europe, but ventriculography was not widely accepted as a routine diagnostic technique.

Stimulated by Sicard's work, Moniz, at that time Professor of Neurology in Lisbon, began to investigate methods of visualizing brain structures by rendering them radiopaque. He first attempted to use oral bromide compounds, based on the knowledge that bromide salts were opaque, and, as evidenced by their sedative effect, probably selectively taken up by the brain. He administered as much as 40 gm of lithium bromide to patients without result.

His next step was an attempt to visualize cerebral vessels with a radiopaque contrast medium. The idea was not entirely novel.\textsuperscript{6} Shortly after Roentgen discovered the x-ray in 1895, Haschek and Lindenthal\textsuperscript{12} in Vienna produced radiographs of blood vessels by injecting opaque solution into cadavers. In 1923, Berberich and Hirsch in Germany\textsuperscript{1} used strontium bromide to obtain arterial and venous angiograms of the arms. Later Brooks\textsuperscript{8} developed a similar technique for outlining the vessels of the legs with sodium iodide. To inject cerebral vessels in the living patient was, however, a more audacious venture.

Apparently Moniz was not aware of this previous work, since he began by studying the opacity of several bromide solutions. He finally selected strontium and lithium salts which were easily visualized through the calvarium. He then verified the local toxic effect of these substances, first in dogs and subsequently in patients with epilepsy and post-encephalitic Parkinsonism. He was familiar with the hazardous effects of intracarotid injections, which had been performed for several years in the treatment of lues of the nervous system.\textsuperscript{5} He performed the first angiograms in dogs in 1926, using a 100\% solution of strontium and lithium bromide (Fig. 1).

Moniz then proceeded to visualize the cerebral circulation in cadavers. Specimens obtained from the pathology department had to be transported in his limousine through the streets of Lisbon to an x-ray laboratory situated in another point of the city. Moniz comments that he was always concerned that an accident might reveal

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**Fig. 1.** Angiogram obtained in a dog in 1926, using strontium bromide.
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what he was actually carrying. The cadaver studies were excellent, and Moniz found the normal anatomy of cerebral vessels to be quite different from descriptions based on dissected specimens. He noted the normal curvatures of the internal carotid artery and coined the terms "carotid siphon" and "Sylvian vessels" that are still in use today.

Commenting on this discovery, an editorial in Lancet remarked that it was likely that these curvatures played "a considerable part in insuring a steady nonpulsating stream of arterial blood within the cranium."

In early 1927, he finally tried his method in patients, using a 70% strontium bromide solution. The results, however, were rather disappointing: the patients moved, the bromide solution extravasated, and two patients developed a transient Horner's syndrome. He then decided to surgically expose the vessel and inject the contrast medium under direct visualization. The injection was finally successful in his sixth patient, but the patient died a few hours later. Because of this setback, Moniz discontinued his research for a time. He attributed the fatality to the contrast material and later resumed his investigations using 25% sodium iodide.

His eighth arteriography procedure was in a boy with severe intracranial hypertension. The contrast medium stopped at the supraclinoid portion of the internal carotid artery and the procedure was considered a technical failure. Moniz later remarked on the delay of circulation of contrast due to increased intracranial pressure and attributed this to compression of the carotid artery by a tumor or ventricular dilatation.

On June 28, 1927, on Moniz's ninth attempt, he was able to produce an acceptable picture of the human intracranial circulation in a living patient (Fig. 2). By comparing this study to normal patterns established from cadaver injections, he localized a lesion in the region of the sella turcica.

The following month (July 27, 1927) he described his new technique to the French Neurological Society in a paper entitled "L'encéphalographie artérielle, son importance dans la localization des tumeurs cérébrales." Before his presentation he showed his results to Babinsky and Sicard. Sicard was examining a patient and remarked how important it would be to have a method to diagnose cerebral tumors similar to myelography for spinal cord lesions. Turning to Moniz, who had just arrived, he asked him if he was bringing to the meeting something new to help localize brain tumors. Encouraged by this opportune question, Moniz promptly showed him his angiograms.

At the meeting his communication was received with great interest and Babinsky stated that if the carotid injections proved innocuous, they should all be grateful for the discovery that "would enable us to localize intracranial tumors, the site of which is often difficult to determine."

A second presentation was made to the Académie de Médecine a few days later. Another angiogram had been sent by train from Lisbon the day before. The study was obtained postmortem and clearly delineated a temporal mass (Fig. 3).

In the following years, Moniz and his group worked to further define the applicability of their method and to clarify a variety of abnormal vascular patterns. By 1929, he had recognized the distinct angiographic picture of different types of tumor and felt that this would be helpful in the diagnosis.

Through a fortunate technical "error" he obtained the first views of the venous circulation in 1931. He then proceeded to
By the time his second book was published in 1934, he had written 112 papers on the subject of angiography. His original contributions included the definition of displacements of cerebral vessels by supratentorial mass lesions in various locations, the angiographic picture of subdural hematomas, the pattern of ventricular dilatation, and the diagnosis of carotid artery thrombosis. He also studied the anatomical variations of the circle of Willis, remarking that the posterior cerebral artery arose directly from the internal carotid in at least 25% of normal subjects. He investigated the arterial and venous circulation of the posterior fossa by direct injection of the subclavian artery. Members of his group were the first to perform aortography by direct injection and to obtain angiocardiology. They also developed an apparatus which they called "radiocarousel" that took six serial angiograms at 1-second intervals.

Although Krause had called attention to the importance of cerebral angiography as early as 1928, and Frazier had noted that there was no reason why the cerebral vessels could not be outlined as clearly as the peripheral ones, acceptance of cerebral angiography as a tool for neurological diagnosis was surprisingly slow. The first angiogram outside Portugal was performed by Dott in 1929, demonstrating an arteriovenous malformation. Löhr and Jacobi were instrumental in the promotion of the technique in Germany and were the first to combine angiography and pneumoencephalography.

The introduction of angiography in the United States proved even more difficult than in Europe. Two factors are frequently mentioned to explain this. The first is that thorotrast, a colloidal thorium dioxide solution used as a substitute for sodium iodide, was suspected of toxicity by the American Council on Pharmacy as early as 1932. In addition, angiography, as practiced by Moniz, required a minor surgical procedure. The latter problem was later solved by Shimizu and Loman and Myerson, who showed that equally satisfactory pictures could be obtained by percutaneous injection. In 1940, a new organic iodide compound which proved to be an innocuous contrast medium was introduced by Gross. As late as 1951, it was still felt by some that angiography as a neurosurgical diagnostic technique was second in importance to ventriculography.

Moniz understood the necessity of publishing his results in English and did so early in the course of his work. Reporting his experiences in the Archives of Neurology and Psychiatry, he mentioned that despite a mortality of only 1.5% in a series of 350 cases, the "distrust persisted." In 1931, an editorial in Lancet stated that it seemed "as if the field of usefulness of the method would be narrowly circumscribed." Two years later, the same journal noted that it was "doubtful whether cerebral angiography will replace ventriculography as the main accessory method available in the diagnosis of intracranial tumors but in vascular tumors, angiomatous malformations and intracranial aneurysms, it seems to give more precise information."

Although continuing to work with angiography, Moniz turned his attention to more therapeutically oriented fields. Prefrontal leukotomy was first performed in December, 1935, and his first book on the subject was published a few months later in Paris. In contrast to angiography, psychosurgery was rapidly accepted and became actively practiced throughout the world. In the United
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States this was due largely to the efforts of Freeman and Watts,\textsuperscript{10} and large-scale trials such as the Columbia-Greystone project.\textsuperscript{17} Moniz tried without success to devise a surgical treatment for Parkinson's disease consisting of injecting alcohol into the white matter underlying the motor cortex.\textsuperscript{21}

From the time of his earliest work in angiography he was joined by Almeida Lima who became his closest associate and collaborator. Moniz was incapacitated by severe gouty arthritis, and left all the neurosurgical work to his trusted colleague. In 1939, Moniz was working on a monograph on angiography when a schizophrenic patient attacked him, inflicting several near-fatal gunshot wounds. Sometime later Foerster, himself severely ill, wrote to him:

"I hope you are happy with your monograph. There is no need to tell you that it is a magnificent work, a monument "aere perenius." I would be happy to hear from you, your time permitting, so I can learn of your health and your work. For you are tireless and fruitful as an apple tree."\textsuperscript{21}

Until his death in 1955 Moniz remained active, writing prolifically on medical and literary topics. The diversity of his interests is well illustrated by the books he published on Portuguese literature as well as on such subjects as the history of playing cards. His book on sexual life, audaciously written at the turn of the century has remained a bestseller and the two autobiographies are a delight to read. Probably no one has described him better than Dott:

"He was a kind, cultured, Portuguese gentleman of quiet, serene disposition, but with a flair for active leadership; an historian, a politician and a gourmet; a doctor of medicine and primarily a clinical therapist—one who viewed his patients' suffering with intolerance—who ardently desired to help the sick."\textsuperscript{6}

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