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This Week's Citation Classic™

French J D, Verzeano M & Magoun H W. A neural basis of the anesthetic state. *Arch. Neurol. Psychiat.* 69:519-29, 1953.
[Veterans Administration Hosp., Long Beach, and Depts. Surgery and Anatomy, Univ. California Sch. Med., Los Angeles, CA]

Earlier studies had identified areas of the central core of the brain stem, differentiated from the primary motor and sensory path-ways, which, when stimulated facilitated or inhibited motor activity and aroused sleeping animals. This paper found that the loss of wakefulness and motor activity, induced by anesthetic agents, resulted from their blockade of these central brain stem mechanisms. This observation provided an initial understanding of the physiological processes involved in the anesthetic state. [The ***SCI***® indicates that this paper has been cited over 275 times since 1961.]

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"H.W. Magoun published the fundamental information leading to this *Citation Classic,* which lists my name first, and must be recognized as an essential coinvestigator in the work. Magoun and I became friends in 1946 in Chicago. He was a member of Northwestern's Institute of Neurology; he had revived use of the Horsely-Clarke stereotaxic instrument, disregarded for decades by scientists. With the instrument, stimulating or recording electrodes could be inserted into deep centers of the brain. Magoun was also a regular visitor at the Illinois Neuropsychiatric Institute where Percival Bailey was my preceptor.

"In 1944, Magoun published the first of a notable series of research reports which were to identify functional capabilities exhibited by the central reticular formation of the brain stem.[1] Stimulation of one portion elicited facilitation of motor activity while excitation of another led to motor inhibition. In 1949, he and a visiting scientist from Italy, G. Moruzzi, discovered that ascending influences of the same general region induced EEC and behavioral arousal in sleeping animals.[2] Later, it was found that lesions of this region led to coma.

"In 1950, Magoun and I came together again at the Veterans Administration Hospital in Long Beach, California, where I was chief of neurosurgery. Jointly, a growing number of laboratories were established there to provide research facilities for the many neuroscientists attracted to UCLA's new school of medicine, then being built in Los Angeles. Marcel Verzeano, one of these investigators attracted to Long Beach, had a special competence in electronics, a valuable asset in this work.

"The Long Beach laboratories were a beehive of activity at that time. Many of us were interested in the reticular formation and its functions in wakefulness and sleep. The next logical step was to find out how anesthetic agents influenced these brain stem mechanisms for wakefulness and motor modulation. The experiments, which occupied the better part of a year, indicated that loss of wakefulness and accompanying muscular changes during the anesthetic state were the result of selective action of the agents administered upon the reticular formation. The high density of cellular junctions in the area, in contrast to the simpler structure of the primary motor and sensory pathways, appeared to provide it with a special sensitivity to the drug action.

"There were a number of reasons for the interest aroused by the paper. First, it appeared during the surge of research interrelating the reticular formation with behavioral states. In addition, the title suggested a clinical relevance of the work which may have attracted the attention of the medical profession. In this connection, perhaps the findings offered a prospect of attaining better control over anesthetic procedures.

"Unfortunately, the exciting days at Long Beach gradually came to an end for most of us. Magoun soon became tied up on the UCLA campus with pressing responsibilities in establishing a department of anatomy and a Brain Research Institute; somewhat later I followed him there as director of the Institute. Verzeano is now professor of psychobiology at the University of California, Irvine.

"It is 28 years since this paper was published and there is still much to be learned from further investigation of neural mechanisms involved in drug-induced states which will contribute substantially to the effectiveness and safety of anesthesia."

1. Magoun H W. Bulbar inhibition and facilitation of motor activity. *Science* 100:549-50. 1955.
2. Moruzzi G & Magoun H W. Brain stem reticular formation and activation of the EEC *Electroencephalogr. Clin. Neuro.* 1:455-73, 1949.