

In Memoriam

Pierre Gloor (1923–2003): An Appreciation

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On October 24, 2003, the world's neuroscience community lost Pierre Gloor, one of its most influential leaders in epilepsy research. Gloor passed away peacefully at the Montreal Neurological Institute and Hospital (the "Neuro") of McGill University, where he had worked relentlessly between his arrival to Canada in 1952 and 1994, when he was felled by a severe stroke. A native of Basel (Switzerland), Gloor received his medical education at the University of Basel and did his resident training in Neurology and Neurosurgery at l'Hôpital Louis Pasteur in Colmar, France. In 1952, he joined the Montreal Neurological Institute as a fellow in the Neurophysiology Laboratory and worked with W. Penfield and H. Jasper. At that time, the Neurophysiology Laboratory, located in a relatively small area on the 7th floor of the Neuro, was crammed with research fellows who would shape our knowledge on brain function under normal and pathological conditions in the years to come (Fig. 1).

In this early period (1952–1957), Gloor explored by electrophysiological means the connections of the amygdala. He found that this limbic area projected intensely to a large brain region comprising the basal core of the forebrain and midbrain extending to the hypothalamus and the brainstem tegmentum. Data originating from these experiments have, indeed, stood the test of time. They were included in Gloor's Ph.D. thesis, submitted in 1957, and became a chapter in the first edition of the *Handbook of Physiology* published by the American Physiological Society (1). This chapter has been much quoted over the last four decades, even though our knowledge on the anatomy and function of the amygdala has enormously increased since 1960, when it was published.

The link of the amygdala with a disparate number of physiological and pathological conditions was probably congenial with Gloor's ability to explore the intimate function of different brain systems such as the hippocampus and the hypothalamus. During the 1960s, he undertook a series of pioneering studies aimed at characterizing the responses of hippocampal and dentate neurons to stimulation of amygdala and entorhinal cortex (2,3). He demon-

strated that these limbic structures contacted the apical dendrites of hippocampal pyramidal neurons and dentate granule cells through excitatory synapses, whereas stimulation of the fimbria engaged mostly the basal dendrites. The laminar profile of these responses demonstrated that hippocampal cells behave as dipoles. Similar conclusions were drawn at the same time by Per Andersen in Oslo (Fig. 2). Gloor's studies also identified some intriguing phenomena that accompany hippocampal electrographic seizures; he found that epileptiform discharges were associated with DC shifts that may play a significant role in seizure maintenance (4). These events are presently explained, at least in part, as reflecting extracellular potassium accumulation.

During these years, Gloor remained focused on the study of amygdaloid connections. He demonstrated that ventromedial hypothalamic neurons receive excitatory and inhibitory inputs from the amygdala basolateral and the corticomedial nucleus, respectively (5,6). Hence these experiments led to the identification of the ability of amygdaloid outputs to exert a dual influence on hypothalamic activity. These studies also clarified how epileptic discharges originating from limbic areas can elicit a variety of autonomic and behavioral responses.

A fundamental characteristic of his investigative approach was the careful analysis of the clinical and neurophysiological features of epileptic syndromes. Gloor used this clinical information to formulate specific hypotheses to be tested in the experimental laboratory. In turn he carefully used the latest experimental results to bear on clinical decisions. An example of this approach can be found in his identification of primary generalized epileptic disorders with spike-and-wave discharges as "corticoreticular epilepsies." The rationale behind this choice is detailed in a review chapter that was written in 1978 (7). I quote a few passages:

About 10 years ago I received an invitation from Dr. Gastaut to go to Marseille to present a review of the neurophysiological basis of generalized seizures termed



FIG. 1. Fellows of the Neurophysiology Laboratory of the Neuro in 1952. Front row: Annie Courtois, Doris Oeconomos, William Feindel; middle row: Guss Stoll, Herbert Jasper, Cosimo Ajmone Marsan; Back row: Guy Courtois, Pierre Gloor, John Hunter, Kenan Tukul, David Ingvar, Maida Tukul, Jake Hanbery.

“centrencephalic.” I suspect he selected me for this assignment because I came from the Montreal Neurological Institute and he expected that I would review the clinical and experimental data which supported the centrencephalic hypothesis of generalized seizures. Originally that was exactly what I intended to do. After reviewing many experimental and clinical studies . . . , I came to the conclusion that it was no longer tenable to conceive of the mechanism of generalized seizures in terms of either a purely centrencephalic or purely cortical mechanism Rather than to look upon the “centrencephalic” and upon the “cortical” hypothesis as being mutually exclusive, I began to explore the notion that generalized epilepsy was dependent upon more complex mechanisms which involved both cortical and subcortical structures Some abnormal interaction between these two levels was thought to be responsible for the conditions, but at that time it was not very clear to me how this abnormal interaction between the two levels could take place. In the light of this rather vague hypothesis, I proposed the term generalized cortico-reticular epilepsies for generalized epileptogenic conditions associated with bilaterally synchronous spike and wave activity (8,9).

It soon became imperative to search for an experimental model of which this new concept could be tested.

The model selected by Gloor was generalized penicillin epilepsy in the cat. This model was the focus of his experimental studies for more than two decades, and I was fortunate to work with him on many of the experiments that were aimed at identifying the relative contributions made by thalamic and neocortical networks to generalized spike-and-wave activity in cats. Most of the original findings obtained in penicillin-treated animals have been recently confirmed by other researchers. Once more, these studies have demonstrated the correctness of his clinically based intuitions.

Proof of Gloor’s unique ability to synthesize clinical and experimental evidence and to pose straight questions also is found in a letter he sent to Dan McIntyre to summarize an invited talk to be given at the annual meeting of the American Epilepsy Society in 1994. This letter, which was written just a few days before his debilitating stroke, identifies questions on temporal lobe epilepsy that are as yet to be answered. I quote:

I believe what I shall do is to stress that even though we know that most temporal lobe seizures in humans originate from

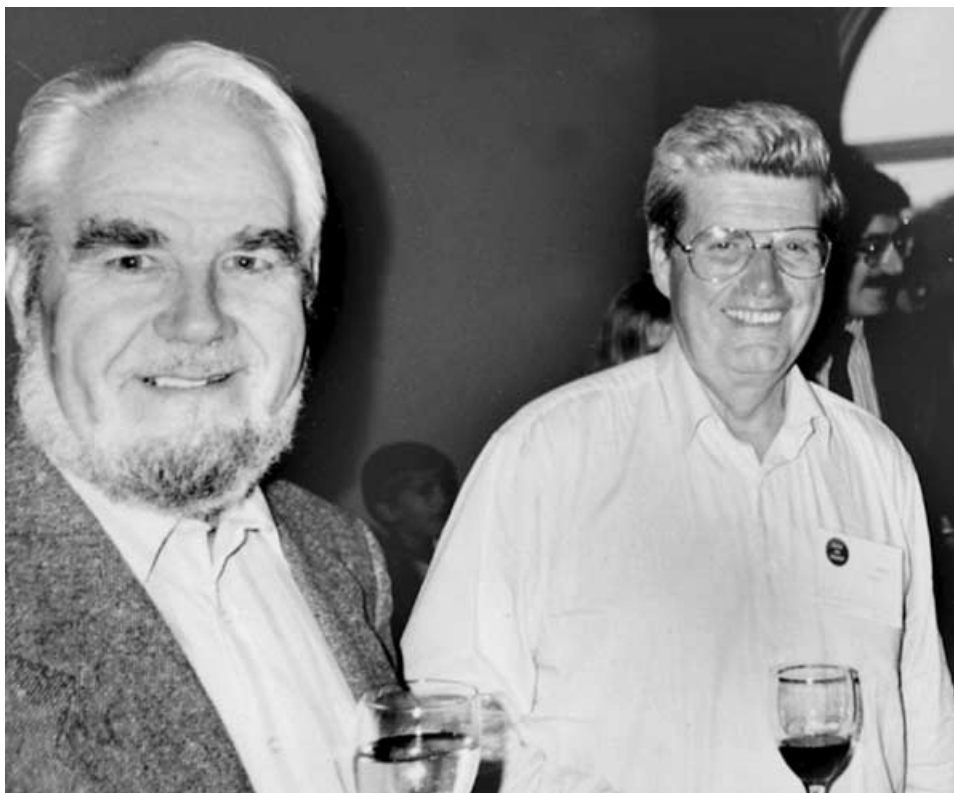


FIG. 2. Pierre Gloor with Per Andersen at the Focus on Epilepsy Symposium I, which was held in St. Adele (Quebec, Canada) in the summer of 1991.

the mesial structures, we are far from understanding which structures are essential or play what role, which is or are the sites of seizure onset and which are the routes of propagation of the seizure discharge. There has been, in my opinion, a simplistic view that the hippocampus is possibly the sole center of action. Hippocampal sclerosis is certainly the most outstanding neuropathological finding in resected temporal lobes of temporal lobe epileptics. And since patients with proven hippocampal sclerosis do best after surgery, the conclusion was that is the sclerotic hippocampus that is the site of origin of the seizures. This may be so, but remains unproven and there are difficulties with this explanation.

... the experimental neurophysiologists who work on normal hippocampi consistently identify CA3 as the site of origin of discharge in a variety of models of experimental hippocampal epilepsy It is hard to see how in an abnormal, sclerotic hippocampus this could be the mechanism of seizure genesis and propagation with hardly any neurons left in either CA3 or CA1. Relatively well-preserved dentate granule cells apparently then come to the rescue. In hippocampus with destruction of the hilar cells and CA3 neurons the dentate granule cell axons sprout collaterals that innervate the molecular layer of the dentate gyrus There is a catch, however. The dentate granule cells can only project to the hilar cells and CA3 and they are gone. So how does a hypothetical seizure discharge in the dentate gyrus propagate out of the dentate gyrus in a sclerotic hippocampus that lacks hilar and CA3 neurons? the hippocampus may not be the sole or principal player in temporal lobe epilepsy. The amygdala may

play an equally important role It seems therefore that we have to begin to think of a distributed epileptogenic process in the mesial temporal region that includes, besides the hippocampus and the amygdala, the parahippocampal gyrus, the entorhinal cortex and the prepiriform cortex The concept which we should try to form is that of a distributed, although pathologically altered, neuronal network in the mesial temporal region that is responsible for seizure genesis in this area. Such a reorganized network may be intrinsically unstable for reasons we do not yet understand and this instability may be the cause for recurrent seizures.

His definitive monograph, entitled “The Temporal Lobe and Limbic System,” was published in 1997 by Oxford University Press and represented a culmination of his life’s interest in the anatomy and physiology of the temporal lobe and its disorders (10).

Gloor worked closely with the clinical and research teams at the Montreal Neurological Institute in the treatment of epilepsy (Fig. 3). In the early 1960s, he improved techniques to record with sphenoidal electrodes the EEG from mesial temporal structures in epilepsy patients. Then, in the 1970s, he developed the use of depth electrodes for the study of patients with bitemporal epileptiform discharges. Overall these efforts led to the introduction of video/EEG long-term monitoring in conjunction with computerized methods. These analytic procedures were later used in animals to analyze the contribution of



FIG. 3. Gloor reading the electrocorticogram recorded from an epilepsy patient during surgery performed at the Neuro in the late 1980s.

neocortical and thalamic networks to the generation of specific brain rhythms under normal and pathologic conditions.

By all means, Gloor's studies on patients were not limited to technological advancements. Indeed, the outcome of his clinical studies is absolutely remarkable. Just to mention a few, he established a number of prognostic factors that would allow one to assess preoperatively the likelihood of a good or unsatisfactory outcome of epilepsy surgery (11,12). In addition, through recording seizures by depth electrodes and performing stimulation of temporal lobe structures, he identified the anatomic substrates and the nature of experiential phenomena in epilepsy patients, most often with temporal lobe epilepsy (13–15).

Gloor began lecturing at McGill in 1954 to become full Professor in 1968 in the Department of Neurology and Neurosurgery. In 1998 he was designated McGill Emeritus Professor. During his academic career, he was the Director of the Laboratory of EEG and Clinical Neurophysiology. He was a key figure in the training of several neurology trainees and epilepsy fellows, many of whom are now internationally renowned experts. He also took an active part in teaching EEG technologists and in organizing a College program for them, resulting in Quebec, and Canada, having superbly trained EEG technologists. In 1988, the Quebec Association of EEG Technologists organized the "Prix d'Excellence Pierre Gloor."

His work in understanding and treating epileptic disorders earned him a worldwide reputation, as witnessed by several international recognitions that included the Robert Bing Prize, the Michael Prize, the William G. Lennox Award, the Wilder Penfield Award, and the Milken Fam-

ily Foundation Prize. Gloor was president of the Canadian as well as of the American Electroencephalographic Society and of the American Epilepsy Society.

Gloor was a scientist, a discoverer, a humanist, a truly decent man, and from my personal experience, an invaluable mentor. His life work has helped us to progress in understanding brain function. No doubt his prodigious contributions will be appreciated by the world neuroscience community for years to come. Thus let me say once more what ended most of our conversations: "Thank you, Dr. Gloor."

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