HISTORICAL INTRODUCTION

History of the Early Development of Electroencephalography and Clinical Neurophysiology at the Montreal Neurological Institute: The First 25 Years 1939-1964

Herbert H. Jasper

Since I have always considered the EEG department to be a clinical branch of the Department of Neurophysiology (not Neurosurgery) I shall be speaking of the Departments of Neurophysiology and Electroencephalography as one in my historical introduction.

We have always had a fine collaboration with neurosurgeons in both the Neurophysiology and EEG laboratories. Many have been fellows in these laboratories at sometime during their graduate work and training at the MNI. In fact I have found that neurosurgeons make very good neurophysiologists and have made important contributions to research in these departments, as well as in the operating room where we have been able to carry out some remarkable electrophysiological studies of the human brain. Most important was the collaboration with Dr. Penfield for recording electrocorticograms from the exposed cortex of conscious patients in the operating room during neurosurgical explorations for the treatment of patients with focal epilepsy. Later, with Dr. Gilles Bertrand, we were able to carry out stereotaxic microelectrode studies of the firing of single thalamic cells in conscious patients being operated upon for the treatment of Parkinson's disease.

I am going to confine my remarks to the first 25 years of this 50 year history, the time when I was captain of the ship sailing through the seas of the brain waves at the MNI, with some excursions into international waters. I hesitated to try to summarize the work done in the first 25 years in this brief publication. Certainly I cannot do it justice in the space at my disposal.

Fortunately I have been permitted by the editors to include at the end of this manuscript a rather complete list of publications numbering 134 references plus an additional 24 references in the Appendix which can be used to fill in the many activities omitted from this report. Some, but not all, will be referred to by number in the manuscript. Even so, many have been omitted and all of the 55 references to the reports of War Research have been omitted since they were sent mostly to the Canadian National Research Council's special committees on Aviation, Army, and Naval Medical research where they have been kept in their archives.

The second 25 years was guided by Peter Gloor who will no doubt be able to review the highlights of his years at the helm, which has only recently been taken over by Luis-Felipe Quesney.

The First EEG Laboratories at Brown University

It was in the year 1933 that I returned from a two year Rockefeller Fellowship in Paris to establish a clinical and experimental EEG laboratory at the Bradley Hospital of Brown University in Providence, Rhode Island, with the aid of a grant from the Rockefeller Foundation. Our first electroencephalograms were recorded in 1934 on photographic paper with Westinghouse 4 channel mirror oscillographs. Howard Andrews, physicist and electronic engineer from Brown, had made some excellent high gain quiet amplifiers with a frequency range of 1 to 2000 Hertz. He made also a good high gain DC amplifier to record the direct current polarization (DC) underlying the EEG.

When I returned to Paris in the year 1935 to defend my doctoral thesis in physiology at the Sorbonne my first thesis was on the neuromuscular system of the lobster, *Homerus Americanus*. The second thesis was on *"Electroencephalographie chez l'Homme"*.

After a successful examination I went to visit Hans Berger in Jena, and Kornmuller and Tonnies in the Brain Research Institute of Oscar and Cecile Vogt in *"Buch bei Berlin"*. I also visited Grey Walter in London, and Adrian in Cambridge before returning to continue our work at Brown University in Providence, RI. I had brought several rolls of film with me so that we could compare results in the various European laboratories.

We were soon joined by Margaret Rheinberger from John Fulton's laboratories at Yale to help us with our implanted electrode experiments on unanesthetized animals. We soon observed

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the generalized arousal response and EEG patterns of sleep in cats. We learned to recognize changes in the EEG when the cats needed to relieve themselves which we called the "cat box effect". Both local and generalized responses to sensory stimulation were observed, giving us a much more dynamic view of the electrical activity of the brain than that which had been observed before in anesthetized animals. This was over ten years before Moruzzi and Magoun described the ascending reticular activating system of the brain stem. We had also observed the changes in the EEG during sleep both in man and in experimental animals. We had even observed sleep tracings from Albert Einstein while visiting the laboratories of Arther Loomis and colleagues in Tuxedo Park, New York.

We then established an active clinical EEG laboratory for the study of epileptic patients, behavior problem children, traumatic brain lesions, and various nervous and mental diseases in adults and children. We were aided in this early development by friendly and somewhat competitive collaboration with our colleagues at Harvard nearby; Alexander Forbes, Bill Derbyshire and Donald Lindsley, Hallowell and Pauline Davis, Fred and Erna Gibbs, and William Lennox.

First Encounter with Wilder Penfield, 1937

I had heard of the opening of the Montreal Neurological Institute in 1934, and Penfield's Harvey Lecture on "The Cerebral Cortex and Consciousness" in 1936. We invited him to give us a lecture at one of our weekly seminars in the Psychology Department at Brown, directed by Leonard Carmichael. We were fascinated by Penfield's observations of responses to electrical stimulation of the exposed human brain during operative exploration for the treatment of focal epilepsy. I thought immediately of the possibility of recording the electrical activity directly from the exposed cortex in these patients.

Following the lecture Penfield came out to visit our laboratories at the Bradley Hospital in East Providence. He was interested but rather skeptical of the possibility of localizing epileptogenic lesions from electrical records taken from the scalp surface. I replied that we would never know until we tried.

The Move to Montreal, 1937-1938

Penfield finally agreed to operate on a couple of my patients on a trial basis, if I would bring them to Montreal with the recording equipment necessary for taking electrocorticograms in the operating room. I began commuting between Providence and Montreal in the year 1937.

I was given a warm welcome by the staff and fellows of the Institute as well as by the Penfield family. We spent week-ends skiing in the Laurentian mountains in winter, and sailing on Lake Memphremagog in summer. I also made the acquaintance of a charming nurse, Miss Margaret Goldie (Figure 1), who took care of one of my behaviour problem epileptic boys by the name of Sammy Corozza who raised hell on the children's ward at the time. Fortunately he was operated upon with fairly good results as I found thirty years later when visiting him as a successful business man in New England, living in Providence, Rhode Island.

Establishment of Laboratories of Electroencephalography and Neurophysiology at the MNI, 1938-1939

My move to Montreal was made possible by Penfield's friendship with Alan Gregg, then in charge of medical sciences in the Rockefeller Foundation. He was able to get my operating grant transferred from Brown to McGill, with additional matching funds for building an addition to the MNI to make room for our laboratories which had not been considered in the original plans of the Institute. Matching funds were also raised by Penfield through the generosity of private donors and the City of Montreal.

The new building, an annex on the ground floor, was completed by January 1939 so that we could have the formal opening shortly thereafter. This was attended by a distinguished group of pioneers in Electroencephalography from the United States and Canada. Those attending the opening ceremonies are shown in Figure 2.

The Opening Ceremonies and the Beginning of the EEG Ski Meetings in the Laurentian Mountains in February, 1939

Following the opening ceremonies, and a tour of the Institute, we all went to Domaine D'Esterel in the Laurentian mountains for a symposium and skiing, including a race among all participants who wished to enter. This was the first of a long series of EEG Ski meetings. They attracted so much interest that they were repeated each winter, drawing many of the leading workers in electroencephalography and neurophysiology from the United States and Canada and some from Europe.

Figure 1 — Nurse Margaret Goldie (see tribute, Jasper[129]).

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When the Eastern EEG Association was formed following the war, they were able to take over the running of the ski meetings as a part of their program of regular annual meetings, which has continued as a tradition ever since. This was the forerunner of similar EEG ski meetings in Europe and in the Western United States.

Establishment of the EEG Department; Prewar Studies

The original EEG department, in a specially designed building attached to the basement of the MNI, contained three excellent electrically and sound shielded rooms with double windows permitting observations of the patients while recording from outside. One of these rooms was built on a separate foundation to eliminate mechanical vibrations from the building, a feature which proved of critical importance for some microelectrode studies on nerve tissue cultures later on. There was also plenty of open space for patient preparations, offices, and a large area in the back for setting up special experiments. This was used during the war for a large animal centrifuge to be described later.

In spite of the gathering clouds of World War II fifty years ago we were able to work effectively in these new EEG laboratories, and in the neurophysiological laboratories on the 7th floor, due to the collaboration of outstanding research fellows and staff at the MNI. In the EEG department the collaboration of Jack Kershman (neurologist and neuropathologist) and Andrew Cipriani (electronics engineer and MD.) were of critical importance, (Figure 3). Andy Cipriani made all of our amplifiers and even the 4 channel ink writers, winding the coils himself. Jack Kershman helped in the recording of EEG tracings and joined in the correlation of EEG findings with clinical and neuropathological findings on the patients being examined.

We were all inspired by Dr. Penfield's dream of a truly multidisciplinary neuroscience Institute, combining basic research laboratories in neuropathology, neurophysiology, neurochemistry, neuropsychology, neuroradiology with clinical neurology and neurosurgery, working together as a team. It was the achievement of this dream that attracted fellows from all over the world for research and training.

EEG Classification of the Epilepsies with Jack Kershman

Jack Kershman and I, with the help of nurse Margaret Goldie and many fellows and technicians, were able to carry out about 1000 EEG examinations on over 500 epileptic patients during the first year. Each patient was given a thorough clinical examination, with radiological examinations and blood chemistry and metabolic studies when indicated.

Over one half of the patients were admitted for more detailed study and consideration in our epileptic conferences for possible neurosurgical exploration. The results of these initial studies were published with Jack Kershman under the title of "Electroencephalographic classification of the epilepsies".[3] About one-half of these patients were considered to represent one or another form of generalized epilepsy.

First Publication on EEG in Epilepsy with Penfield, 1941

The technique of electroencephalography and a description of our initial EEG studies were summarized in Chapter XIV of the book by Penfield and Erickson, "Epilepsy and Cerebral Localization" published in 1941.[5] In this chapter I described the techniques used in the EEG developed at the MNI, including the 10/20 electrode system, and sphenoidal electrodes, which became standard methods in nearly all laboratories in later years. The various wave forms found in epileptic patients were

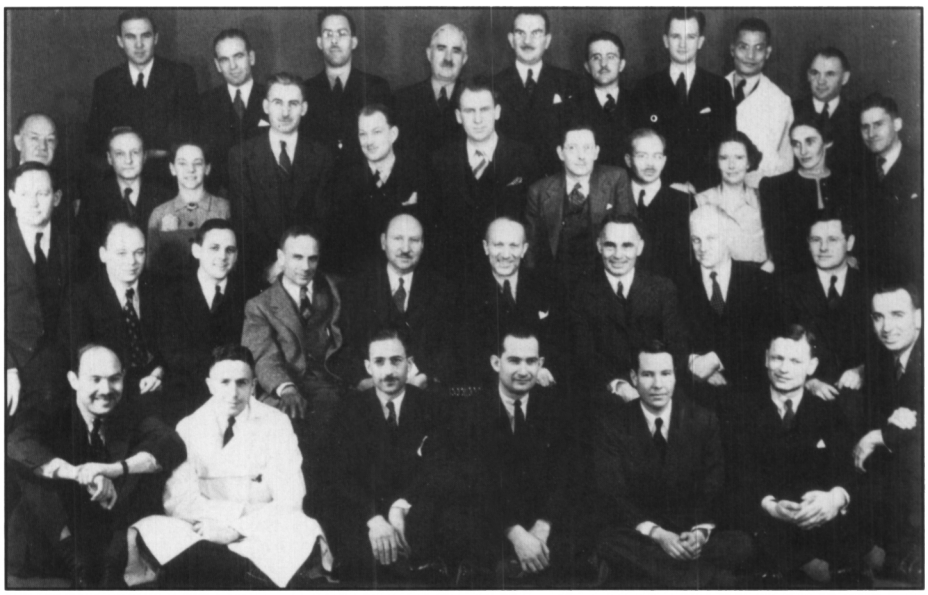

Figure 2 — Opening Ceremonies of the EEG and Neurophysiology Laboratories at the Montreal Neurological Institute, February 24, 1939.
(L to R) Front Row: R. Schwab, S. Humphreys, H. Jasper, A. Cipriani, G. Hobart, N. Fraser, W. Cone.
2nd Row: L. Nims, D. Lloyd, J. Hughes, S. Cobb, N. Harvey, W. Penfield, A. Loomis, A. Forbes, H. Davis.
3rd Row: C. Russel, N. Peterson, M. Rheinberger, E. Baldes, G. Hall, T. Erickson, J. Goodwin, T. Case, M. Harrower, Mrs. R. Schwab, A. Elvidge.
Top Row: H. Andrews, J. Evans, D. Solandt, F. McKay, J. Kershman, R. Smith, D. Lindsley, Y. Chen Chao, S. Dvorkin.

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also illustrated in relation to their clinical findings, as well as electrocorticographic observations taken with Dr. Penfield from the exposed cortex during surgical explorations.

In addition I find to my surprise that there were also another eight publications in EEG and neurophysiology from work done in these laboratories just before we all became preoccupied with war research. These included techniques for the recording of pH, cerebral blood flow and blood pressure during experimental epileptiform seizures (with Cipriani[1]). The use of such techniques on experimental epileptiform seizures in animals was published with Ted Erickson.[4] There was a study of the EEG in acute head injury with Jack Kershman and Arthur Elvidge,[2] and another study of head injury with Wilder Penfield[11] as a beginning of our program in war research.

In collaboration with Charles Shagass, a student from the department of psychology at McGill, we were able to carry out some interesting studies in conditioning of the EEG in man.[7,8] In collaboration with Roy Swank, who had recently joined as a neurology fellow from Boston, we studied the electrical activity of the brain in thiamine deficient pigeons.[9] I had known Roy before when he was in Boston and I was a frequent visitor from Providence, RI.

War Research, 1940-1945

World War II broke out in earnest in 1940, after a year of the "phoney war". It really began with Hitler's invasion of Poland and Czechoslovakia, followed by the invasion of France, and Norway, leaving England under attack after the defeat at Dunkirk. Following the French armistice England was alone, but soon was joined by Canada and other members of the Commonwealth. We had to mobilize rapidly and to provide an adequate medical corps for the Army, Navy and Air Force.

Figure 3 — John Kershman (left) and Andre Cipriani (right), the two most important associates in the founding of the EEG and Neurophysiology departments at the MNI (see text).

The entire Institute was given over to war research and preparation for taking care of the casualties, partly with the help of a Quanson hut erected back of the Institute building. Our laboratories were engaged in a variety of war research projects including;

Blackout in Air Force Pilots

The physiology of "black-out" in pilots subjected to high G forces in combat was studied with experimental animals on a centrifuge installed in the EEG Department. We recorded the EEG, the electroretinogram, intracranial and intraocular pressures, arterial and venous blood pressures, and moving pictures of pial blood vessels while the animals were revolving on the centrifuge to simulate the G forces experienced by pilots in flight. A protective anti-G suit was developed for monkeys upon which was based the principle of the anti-G suits used in combat by American and Canadian pilots in the Battle of Britain.

Seasickness

Experimental studies of sea sickness and development of the Canadian Navy anti-seasickness remedy for use by Canadian forces in the invasion of France on D day.

Brain Edema

Studies of the mechanisms of edema and swelling of the brain were carried out with Dr. K.A.C. Elliott; production of an artificial spinal fluid, (Elliott's solution) used in neurosurgery.

Air Ambulance Transport

Air ambulance transport of patients with brain injuries studied by placing patients in a decompression chamber. We helped to establish air transport of wounded for the Royal Canadian Army Medical Corps (R.C.A.M.C.).

Treatment of Burns

With Dr. Cone we studied the treatment of burns, using small piglets from the restaurant "Au Lutin qui Boeuf".

Studies of Electromyography in Nerve Lesions and Nerve Regeneration

We carried out electrophysiological studies of nerve lesions and regeneration in experimental animals and by the use of electromyography in patients with nerve lesions.

Use of Antibiotics on the Brain

With Doctors Cone and Pudenz we carried out electrographic studies of the effect of direct application of antibiotic substances on the exposed brain, finding that some were strong epileptogenic agents, including penicillin and sulfathiazole.

Use of the EEG in Pilot Selection

Trials of the use of the EEG in pilot selection were carried out, finding some with sensitivity to intermittent photic stimulation.

The results of these studies were reported to the National Research Council, with a few additional reports published in outside journals.[13-23,25,29] In addition to these studies I was able to write an overall review on the "Electrical activity of the

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brain" for the Annual Review of Physiology[6] before becoming fully involved in war research.

There were two additional events in 1940 which had a profound influence upon my life at the MNI. I was married to that attractive nurse, Margaret Goldie, mentioned above as one of the principal attractions of the Institute, (ref. 129, Figure 4a). At the same time I entered the McGill Medical School, taking advantage of the shortened 3 year course in order to be qualified in Medicine to help provide greatly needed medical officers for the R.C.A.M.C. and to be better prepared to carry out research on patients with neurological diseases following the war.

Continuing to run the EEG Department as well as the various war research projects described above, with frequent trips to the United States for conferences on subjects of mutual interest or collaboration left me little time for my regular medical studies. However, with considerable help from my good wife and the friendly cooperation of my classmates in the preparation for exams, I managed to graduate in 1943 and depart immediately for military training as an officer of the R.C.A.M.C. Following a period of rigorous training at Camp Pettewawa and then at Camp Borden I returned to the Institute to continue our War Research projects (Figure 4b).

Post War Resurgence of Research in Neurophysiology and Clinical Electroencephalography

Following the war there was a sudden influx of fellows and visiting doctors from many countries to join us in our conferences, clinical training, and research activities. For example, on the very first boat leaving The Netherlands for New York there was a delayed Rockefeller Fellow by the name of Jan Droogleever-Fortuyn. He was an accomplished neuroanatomist from Amsterdam who came with his charming wife, a psychiatrist and poet, and also a consultant to the government on social and labor problems.

After Jan had recovered somewhat from the trauma of living through the Nazi occupation of his country, with near starvation and witnessing the persecution and execution of many of his countrymen, he began his classical studies of thalamo-cortical relations which led us to confirm many of the findings of Morison and Dempsey on the intralaminar recruiting system of the thalamus and its importance in the generalized control of the electrical activity of the cerebral cortex. We were surprised to find also that 3/sec. stimulation of the intralaminar thalamus in lightly anesthetized cats produced a bilaterally synchronous wave and spike pattern similar to that seen in the EEG during petit mal epileptic seizures.[24] This work was reported at the same meeting of the A.R.N.M.D. in 1946 as was the report with Penfield on *"Highest Level Seizures"*.[27]

Electrical stimulation with implanted electrodes in cats and monkeys, carried out with John Hunter, produced what we called the "arrest reaction". It was associated with slight

*Figure 4 — The War Years: 1940-1945; **(a)** Wedding to Margaret Goldie, August 1940 in Guelph, Ontario. **(b)** In uniform, H. Jasper, R. Pudenz, E. Peterson.*

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twitching of the eyes or face muscles which resembled closely a typical petit mal absence attack in man.[38] We thought we might have discovered the site of a pacemaker which could control the bilateral synchrony of the spike and wave discharge, as suggested with Jack Kershman in our studies of the EEG in pure absence attacks.[3]

The American Society of Electroencephalography and the International Federation of Societies for Electroencephalography and Clinical Neurophysiology

In 1946, in conjunction with the annual meeting of the American Neurological Association in Atlantic City, the American EEG Society was organized and they elected me as their first president for a period of two years, 1946-1947. My presidential address, *Charting the Sea of Brain Waves* was published in Science.[35]

In 1947 we held an International Congress in London to form the International Federation of Societies for Electroencephalography and Clinical Neurophysiology, and to establish its official Journal, The EEG Journal. There were only three national societies at that time, France, Great Britain, and the United States.

To my great surprize I was elected president of the International Federation and Editor in Chief of its Journal, "The EEG Journal". The editorial and publication offices of the Journal were established in the EEG department at the MNI, and in the home of Margaret Goldie Jasper as well as in the home of Mrs. Miguel Prados nearby in Montreal.

Mrs. Michaela Prados, a Spanish lady, was the wife of Dr. Miguel Prados, a psychiatrist and accomplished histologist from Cajal's laboratory in Madrid, who had joined our staff at the MNI as a refugee from the Spanish Civil War in the early 1930's. Michaela Prados was an experienced multilingual proof reader working at the International Labor Organization Offices in Montreal. She was willing to join us for the founding of the EEG Journal if she could take over the proof reading in her own home. Living nearby Margaret Goldie could assist her, as well as help with the printing and distribution of the Journal with a local French printing firm by the name of Therien Freres. With excellent cooperation from the printer we developed a very pleasant and efficient organization, Margaret becoming circulation manager. Robert Schwab in Boston was the business manager.

We had the cooperation of an excellent international editorial board, with the help of Grey Walter as chief European Editor, assisted by Storm von Leuwin in the Netherlands. Peter Gloor soon became my assistant in Montreal, and Bob Schwab was replaced by Mrs. Denton as business manager in our Montreal offices.

The Journal started publication in 1949 with a most memorable first volume. Many of the papers in this volume have become classics in the field. I believe it is worth while to list the table of contents for historical interest.

ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY
An International Journal

No. 1 – February, 1949

SYMPOSIUM: Physiological Basis of Epileptic Discharge
Gerard, R. Chairman, Opening Remarks.
Penfield, W. Epileptic manifestations of cortical and supracortical discharge.
Jasper, H. Electrical signs of epileptic discharge.
McCulloch, W. & Darrow, C. Mechanisms for the spread of epileptic activation of the brain.
Elliott, K.A.C. Biochemical approaches . . .
Toman, J. Neuropharmacology . . .
Lennox, W. Influence of drugs on the EEG.
COMMUNICATIONS:
Walter, V.J. & Walter, W. Grey The central effects of rhythmic sensory stimulation.
Monnier, M. *L'electroetinogramme de l'homme.*

No. 2 – May 1949

Davis, H. The Forbes "school" of neurophysiology at Harvard.
Forbes, A. et al. Refractory phase in cerebral mechanisms.
Bremer, F. *Considerationes sur l'origine et la nature des ondes cerebrales.*
Brazier, M.A.B. The electrical fields at the surface of the head during sleep.
Gastaut, H. *Enregistrement sous-cortical de l'activite electrique spontanee et provoquee du lobe occipital humain.*
Gibbs, F. & Knott, J. Growth of the electrical activity of the cortex.

No. 3 – August 1949

Kristiansen K. & Courtois, G. Rhythmic electrical activity from isolated cerebral cortex.
Masland, R., Austin, G., Grant, F. The electroencephalogram following occipital lobectomy.
Ajmone-Marsan, C. & Fuortes, M.B. Electrographic study of the convulsant action of intravenous acetylcholine.
Ajmone-Marsan, C. et al. Influence of ammonium chloride on the electrical activity of the brain and spinal cord.
Clark, S.L. & Ward, J.W. The electroencephalogram in cerebellar seizures.
Hunter, J. & Jasper, H.H. Effects of thalamic stimulation in unanaesthetized animals.
Little, L.C. Changes in the EEG with mesantoin.
Blinn, K.E. & Noell, W.K. Continuous measurement of alveolar CO_2 tension during the hyperventilation test in routine Electroencephalography.
Lorimer, F.M. et al. Path of current distribution in brain during electroconvulsive therapy.

No. 4, November 1949

SYMPOSIUM: Thalamocortical Relationships
Walker, A.E. Introductory remarks.
Rose, J.E. & Woolsey, C.M. Organization of the mammalian thalamus and relationship to the cerebral cortex.
Jasper, H.H. Diffuse projection system; the integrative action of the thalamic reticular system.
Bishop, G. Potential phenomena in thalamus and cortex.
Hayne, R.A., Belinson, L. & Gibbs, F.A. Electrical activity of subcortical areas in epilepsy.
Bremer, F. & Bonnet, V. An analysis of the sensory responses of the arcuate cortex.
Walker, A.E. Concluding remarks.
COMMUNICATIONS:
Moruzzi, G. & Magoun, H.W. Brain stem reticular formation and activation of the EEG.
Lindsley, D.B., Bowden, J.W. & Magoun, H.W. Effect upon the EEG of acute injury to the brain stem activating system.

Grossman, C. Sensory stimulation during sleep.
Epstein, J. & Lennox, M. EEG study of experimental vascular occlusion.

It is obvious from the above table of contents that the first volume of the EEG Journal got us off to a good start. The Journal grew rapidly during the next 12 years when it was sold to the Elsevier Company in Amsterdam who have continued its publication ever since.

The Loss of John Kershman, 1906-1951

The work of the department of electroencephalography at the MNI suffered a serious setback in the Spring of 1951 when John Kershman had a fatal heart attack while attending the annual meeting of the American EEG Society held in Atlantic City in conjunction with the annual meeting of the American Neurological Association. He had just completed the presentation of an interesting paper on Metrazol activation of the EEG when he suffered a major heart attack during the discussion period which was rather animated. He was rushed to hospital in Atlantic City where he struggled bravely for three days for survival without success. Dr. Penfield and I, together with his many friends and family, felt a deep sense of loss of a loyal and greatly beloved friend. The research in electroencephalography, neurology and neuropathology at the Montreal Institute suffered a severe blow since his very productive career had been arrested in its prime. His sincere scholarship, warm human friendship, his sense of humor and great loyalty on all occasions was an important feature of the life of the Neurological Institute as a whole.

As a token of the high esteem shown by his colleagues in the Eastern Association of Electroencephalography there was established an annual John Kershman lecture to be held during its December meeting in New York City in conjunction with the meeting of the American Epilepsy Society and The Association for Research in Nervous and Mental Diseases. These lectures have continued to be an important feature of these December meetings each year.

Stereotaxic Atlas of the Diencephalon of the Cat

In our studies of thalamo-cortical relationships it was necessary to develop a stereotaxic atlas of the diencephalon in order to be able to locate accurately the site of placement for a stimulating electrodes according to the three dimensional coordinates of the stereotaxic apparatus. It was also necessary to be able to confirm the site of stimulation by histological study of the fixed brain and to know which nucleus of the thalamus, basal ganglia, or brain stem is being stimulated. Fortunately we had the assistance of two expert neuroanatomists for the cytoarchitectonic divisions required, Jan Doogleever-Fortuyn and George Olszewski.

In order to make the coordinates as accurate as possible we corrected the location of anatomical divisions successively following each experiment, so that in the end the final Atlas had coordinates based upon an average of many animals, to compensate for experimental variations. The final drawings of the diagrams were made from histological sections by Cosimo Ajmone-Marsan, who was quite skillful with pen and ink drawings.

After we were sure that the coordinates were quite accurate in a series of experiments we prepared the microphotographs of a series of histological sections together with Cosimo's diagrammatic drawings, with an accompanying text for publication since there was quite a demand for an accurate cat Atlas at the time. The first edition was published by the National Research Council of Canada in Ottawa.[65] It became a standard for stereotaxic studies of the cat diencephalon for many years.[106,107] A similar Atlas for the monkey (but without experimental corrections) was then prepared by George Olszewski, which also became a standard for experimental work on the Macacus Mullata monkey.

The Laurentian Symposium on "Brain Mechanisms and Consciousness"

In 1953 the International Congress of Physiological Sciences was held in Montreal. As a satellite of this Congress, and with the help of the Council for International Organizations of Medical Sciences (CIOMS, J.F. Delafresnaye) and with the cooperation of Adrian of England and Bremer of Belgium we organized a symposium on "Brain Mechanisms and Consciousness." It was held at the Alpine Inn at St. Marguerite in the Laurentian mountains.

The papers and discussions of this intriguing age old problem had just been brought to the foreground by Moruzzi and Magoun with their work on the brain stem reticular system and by our work on the thalamic reticular system. Both were related to mechanisms for the control of the EEG and states of consciousness.

The participants in this symposium (Figure 5) included Bremer, Adrian, Gastaut, Penfield, Lashley, Hebb, Morison, Kubie, Moruzzi, Magoun, Jasper, Grey-Walter, Jung, Fessard, Brazier, Hess, Nauta, Olszewski, McK. Rioch and others who helped to make this a most memorable occasion indeed. It was published simultaneously by Blackwells in Oxford England, Charles C. Thomas of Springfield, Mass, U.S.A., and by the Ryerson Press in Toronto in 1954.[66]

Epilepsy and the Functional Anatomy of the Human Brain. Penfield, W.P. and Jasper, H.H., 1954

Also published in 1954 was the book on "Epilepsy and the Functional Anatomy of the Human Brain" written with Dr. Penfield to summarize our work together over the years.[68] The final manuscript of this book was also reviewed together at The Far Hills Inn in Val Morin, in the Laurentian mountains. A photograph taken by Charles Hodge of myself and Penfield on completion of this manuscript shows the pleasure we both had working together on this project (Figure 6). This book has never been revised, and it is still selling well 35 years later. It must have some historical interest!

The Training of Electroencephalographers; Peter Gloor returns from Switzerland

In the 20th Annual Report of the Institute for the year 1954-1955, it is noted that we had trained 79 electroencephalographers since opening in the fall of 1938. There were seven neurophysiology fellows during this year: Drs. Rothballer, Laramendi, Rayport, Sharpless, Morell, Naquet and Gloor. A picture of the EEG and neurophysiology fellow in 1951-52 is shown in Figure 7, with some familiar personalities as they looked 38 years ago.

It was these and many more fellows who were largely responsible for the work in EEG and neurophysiology during

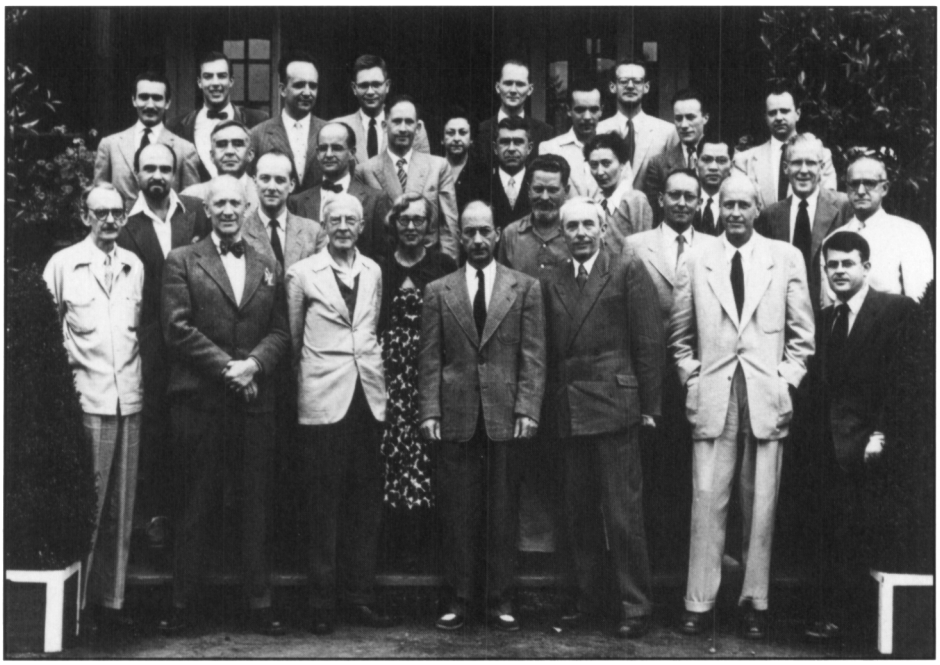

Figure 5 — Brain Mechanisms and Consciousness, International Symposium, The Alpine Inn, St. Marguerite, "les Laurentides", 1953.
(L to R) Front Row: K. Lashley (Harvard), W. Penfield (Montreal), E. Adrian (Cambridge GB), M. Brazier (Boston), H. Jasper (Montreal), F. Bremer (Brussels), H. Magoun (Los Angeles), J. Green (Los Angeles)
Second Row: H. Gastaut (Marseilles), D. McRioch (Harvard), A. Fessard (Paris), R. Morrison (Harvard), R. Hess (Zurich), G. Olszewski (Montreal), W. Grey Walter (Bristol), H. Mahut (Montreal), R. Jung (Frieburg), Cho Lu Li (Montreal), D. Hebb (Montreal), J. Kubie (Yale).
Third Row: C. Ajmone-Marsan (Montreal), R. Livingston (Los Angeles), G. Morruzzi (Pisa), J. Whitlock (Los Angeles), W. Nauta (Boston), J. Delafresnaye (Paris), D. Ingvar (Lund Sweden), R. Buser (Paris), H. Flanagan (Montreal).

the first 25 years. I have listed 190 fellows working in these departments during this time. I would like to take this opportunity to thank them all for their collaboration and friendship. I have been unable to recount in detail many of their important accomplishments but some (24) of their publications have been listed in the Appendix. Some of the most memorable may be listed as follows:

1. Boris Babkin from Leningrad with John van Buren carried out fascinating studies of the cortical representation of feeding behavior.[1]

2. David Ingvar from Sweden carried out important studies of the reproduction of the spike and wave EEG pattern by subcortical electrical stimulation[3] and Hunter and Ingvar worked out the pathways mediating the Metrazol-induced irradiation of visual impulses.[4]

3. Studies of conditioning and learning were carried out by Stepien, Cordeau, and Rasmussen[11,12] and George Majkowski from Poland. Differential delayed learning in monkeys was studied by John Orbach and Helen Mahut from the United States.

4. Peter Gloor carried out his classical studies of the autonomic functions of the diencephalon[2] and the functional anatomy of the Amygdaloid nucleus.[9]

5. Laminar analysis of experimental epileptic discharge in the hippocampus was carried out by Peter Gloor, Luigi Sperti from Italy and Christian Vera from Chili.[14] Foster Redding studied the effect of hippocampal stimulation upon evoked potentials from cerebral cortex.[24]

Figure 6 — Penfield and Jasper with the manuscript of their book "Epilepsy and the Functional Anatomy of the Human Brain" published by Little Brown, Boston, 1954.

6. Juhn Wada introduced the intracarotid Sodium Amytal test for preoperative tests of cerebral dominance. Rovit, Hardy and Gloor[10] and Rovit, Gloor and Rasmussen[14] developed the use of

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this test with the EEG for epileptic patients with uncertain lateralization of their focus of discharge.

7. Roger Broughton carried out some interesting studies of the effect of sleep on evoked potentials in the EEG with Wier-Ewart, and Ebe.[20] With Tsai and Haddad, Gloor also published a study of the value of sleep in the EEG from temporal lobe epileptic patients.[8]

8. Andrew Gorman, from the United States, studied the innervation of the pyramidal tract,[21] and Roy Steinberg studied oscillatory activity in the retina and optic tract,[22] and Alan Rothballer studied the action of several drugs on the ascending reticular activating system.[5]

9. Robert Martin, postdoctoral biophysicist and Charles Branch, fellow in neurosurgery carried out microelectrode studies of excitation and inhibition of pyramidal cells in the cat cortex.[6,7]

10. Finally there was a series of important microelectrode studies of mechanisms involved in experimental spike and wave discharge carried out by Phanor Perot, Bryce Weir, and Dan Pollen[15-19]

Under the able teaching of Lewis Henderson and Lili Prisko, our leading EEG technicians, we trained 49 technicians. We continued to carry out two to three thousand EEG examinations per year on about two thousand patients, about one-half of whom were epileptic.

In the 1954 Annual Report of the Institute it is stated that we had a federal provincial research grant for *"microelectrode analysis of the mechanisms of epileptic discharge in the brain. Drs. Rayport and Gloor are continuing the work begun with Drs. McLennan and Li with this new technique. We hope soon to be able to listen in on the discharge of single cells in the human brain."* This hope was soon realized with Gilles Bertrand who was carrying out stereotaxic microelectrode explorations of the human thalamus during surgery for the treatment of tremor and rigidity in patients with Parkinson's disease. He was guided by the sound of unit cell discharge recorded with a microelectrode in the thalamus when mapping the area to be excised (Figure 8).[125-127]

In the Annual Report for 1954-55 there was the following announcement: *"We are pleased to announce that Dr. Peter Gloor has returned from Switzerland to become assistant electroencephalographer in this department."*

Relations with the National Institutes of Health in the United States

Relations with the NIH in Behesda began even before it was founded, while I was still working in our first EEG laboratories

Figure 7 — Fellows in Electroencephalography and Neurophysiology, 1952
(L to R) Front Row: Annie Courtois, Odoris Oeconomos, William Feindel
2nd Row: "Gus" Stoll, Herb Jasper, Cosimo Ajmone-Marsan
3rd Row: Guy Courtois, Pierre Gloor, Kenan Tukel, Maida Tukel, John Hanbery
Top Row: John Hunter, David Ingvar

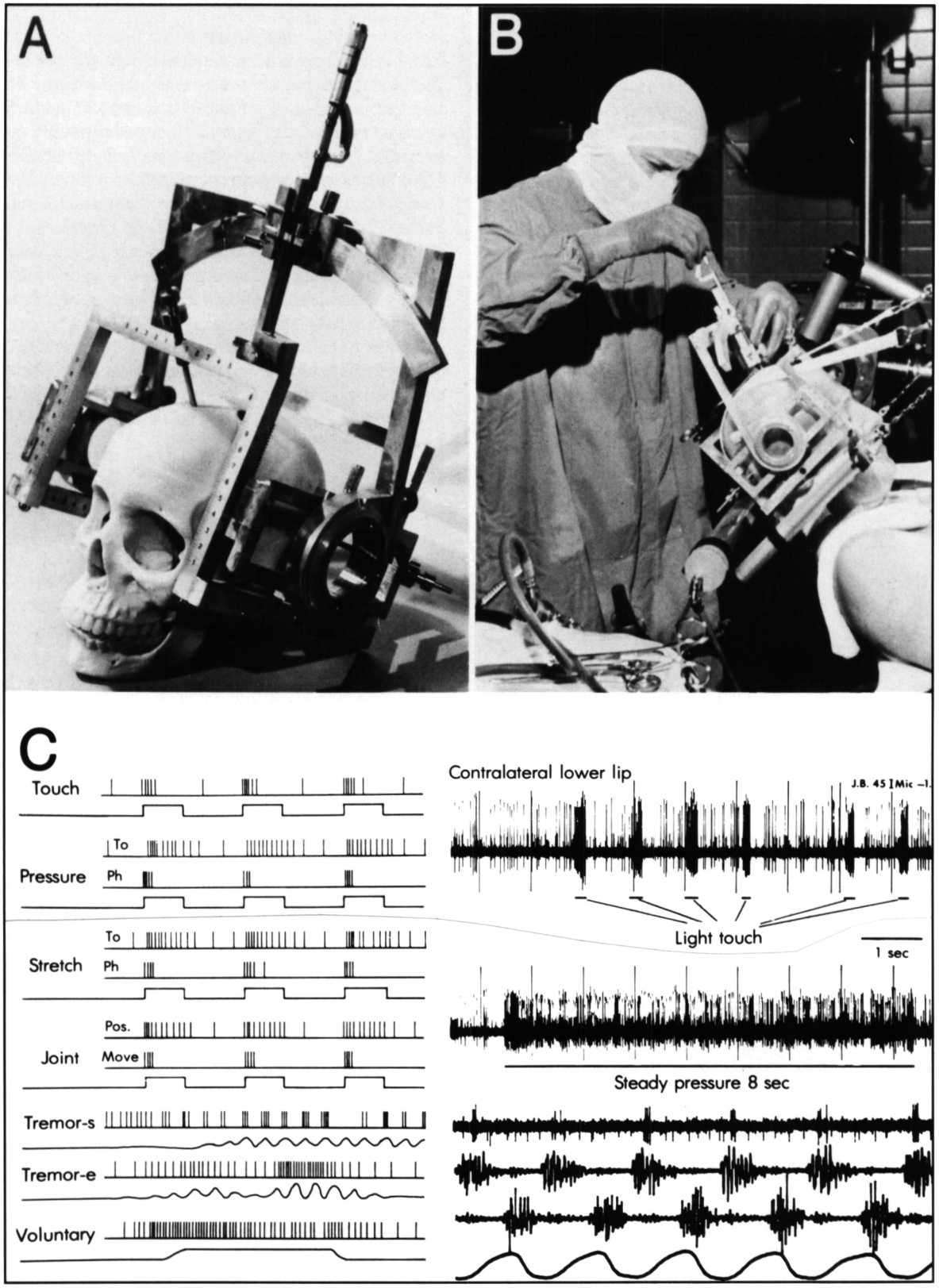

*Figure 8 — Sterotaxic Microelectrode Studies of the human thalamus during surgical treatment of patients with Parkinson's disease with Gilles Bertrand. **A.** Stereotaxic apparatus attached to skull. **B.** Dr. Bertrand, inserting a microelectrode in patient with Parkinson's disease. **C.** Sample records from microelectrodes in thalamus in waking patient, on left are illustrated diagramatically the types of units recorded from different parts of the thalamus, on the right are some actual records of responses to touch, deep pressure, and units firing with spontaneous tremor.*

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at Brown University in Providence Rhode Island. In 1936 there came to our laboratories in the Bradley Hospital an enthusiastic young psychiatrist by the name of Robert Felix. He came to learn something of electroencephalography but brought with him a suitcase full of blueprints for the building of the NIH in Behesda. We spent the days together in the laboratory and the evenings going over the blueprints, both of us excited by the possibilities of National Institutes of Health, including an Institute for Mental Health, and an Institute for Neurological Diseases. The blueprints were not transformed into buildings until after the war, after I had moved to Montreal. We then had the opportunity to help staff the Institute of Neurological Diseases and Blindness (NINDB) from the large number of fellows who came to the MNI for training after the war. A list of the MNI fellows recruited for the NINDB is as follows:

NEUROSURGERY: Maitlin Baldwin, John Van Buren, Cho Lu Li.

NEUROLOGY: Milton Shy, John Lord, William Caveness, Richard Masland (to become director).

NEUROPATHOLOGY: Igo Klatzo, Anatole Dekaban.

ELECTROENCEPHALOGRAPHY AND NEUROPHYSIOLOGY: Cosimo Ajmone-Marsan, Cho Lu Li, William Caveness, Anthony Gorman, Costa Stefanis.

NEUROCHEMISTRY: Donald Tower (to become director).

We were all delighted for the opportunities thus provided for some of our fellows to take part in some of the most important developments of neurological sciences at the NIH.

Microelectrode Studies of Single Cells in Waking Monkeys

Becoming super saturated with EEG records by this time, I was anxious to develop better techniques for unit recording with microelectrodes in waking behaving animals, and possibly even in man. I had concluded that it was necessary to proceed with records of single cells to make further progress in our understanding of brain mechanisms beyond what is possible with the EEG. Consequently, with a couple of research fellows, Gianfranco Ricci from Rome and Benjamin Doane from the psychology department at McGill, we undertook to develop a technique for recording from single cells in monkeys held in a restraining chair without anaesthesia (Figure 9).

We were soon able to acquire a vast amount of photographic records of unit and surface electrical activity from different cortical areas in monkeys, asleep and awake, and during the formation of conditioned responses to various forms of stimuli (Figures 9a and b)

The result from the microelectrodes were clear cut, with little useful information coming from the surface electrocorticograms taken simultaneously. Descriptions of the firing of single cortical cells in the unanesthetized monkeys during sleep and waking, and during the establishment of conditioned reflexes were presented, in part, with Ricci and Doane at the "IVth International EEG Congress" in Brussels in 1957[82] and at the Ciba Symposium on "The Neurological Basis of Behavior" in London in 1958.[86] Finally a more complete presentation of our results was presented at the "Moscow Colloquium on Electroencephalography of Higher Nervous Activity" in 1958.[96] In 1958 there was also a separate report on the patterns of single cell discharge in relation to surface electrocorticograms and responses to sensory stimulation in unanaesthetized monkeys as part of the symposium on the Reticular System held in Detroit in 1958.[88]

These were the first studies of the electrical activity of single brain cells in unanesthetized behaving animals, asleep and awake, responding to various forms of sensory stimulation by conditioned motor behavior, and carrying out intentional voluntary movements. The technique was soon perfected in many laboratories with the aid of computers for programming the experiments and computing the results of the microelectrode records even while the experiments are being carried out. The application of such techniques has permitted a revolutionary new development in the electrophysiology of the brain at the cellular level.

The Moscow Colloquium on Electroencephalography of Higher Nervous Activity, 1958

The Moscow Colloquium was organized by the Academy of Sciences in Moscow together with Henri Gastaut and other members of the executive council of the International Federation of Electroencephalography and Clinical Neurophysiology.[96] It was a most successful and interesting scientific meeting from all points of view. It was edited in Montreal with the help of George Smirnov who was one of the Soviet organizers of the Moscow Colloquium and who was able to spend a year in our laboratories as a research fellow in 1959 following the colloquium.

We were all entertained royally by our Soviet colleagues during the colloquium held in Moscow. They then took us on a train to Lenigrad for a visit to the Pavlovian laboratories there and to the Hermitage Museum and other parts of that beautiful city. After our return to Moscow another group, including myself, were taken to Tbilisi in the Republic of Georgia where we were entertained by Professors Beritashvili, Narikashvili, Roitbac and other members of this famed Physiological Institute.

The International Brain Research Organization, IBRO Paris, 1958-59: Incorporated in Canada, 1960

Stimulated by the intellectual exchanges and warm personal relations with our Soviet colleagues after the final session of the colloquium in Moscow the decision was made to establish an international interdisciplinary brain research organization, hopefully sponsored by UNESCO in Paris. Alfred Fessard and I were delegated to approach UNESCO with a plan for such an organization to be formed within the Natural Science Department of UNESCO.

Our plan was accepted with details being worked out at our first Executive Council Meeting in Paris in 1959. IBRO was then incorporated as an independent, non-governmental international scientific organization by the parliament of Canada in 1961.

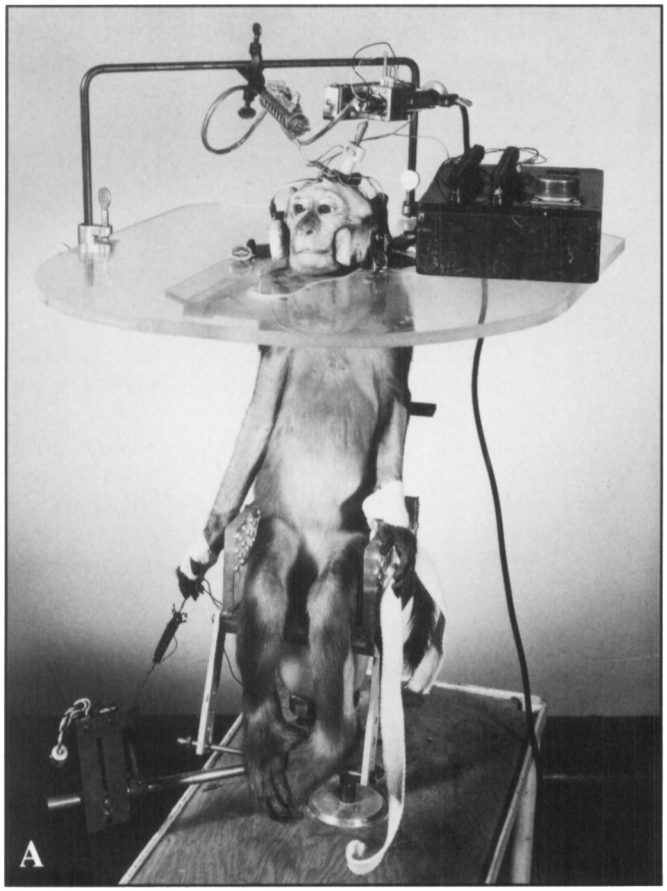
In order to get the organization started I took a sabbatical leave and moved to Paris during the year 1961-62 serving as the Honorary Executive secretary for 3 years.

Peter Gloor takes over the EEG Department, 1961-62

In the Annual Report of 1961-62, Dr. Gloor reported a total of 3,436 EEG examinations carried out in the department. This represented a healthy growth of about 7% per year, with about 40% of the patients being epileptic.

Returning to the laboratory in 1962 I began some intracellular microelectrode studies of cortical cells in cats with Costa

Stefanis, a post doctoral fellow from Athens. We were able to record from pyramidal cells in the depths of the cortex identified by their antidromic responses to stimulation of the pyramidal tract in the midbrain. Electrical activity was recorded simultaneously from the cortical surface immediately above the site of penetration of the microelectrode so that comparisons could be made between the surface electrocorticogram and the intracellular microelectrode records from pyramidal cells beneath. We studied spontaneous rhythms asleep and awake and responses to specific and non-specific afferent stimulation. We carried out a detailed study of recurrent collateral excitation and inhibition following antidromic stimulation of the pyramidal tract in the brain stem. We were both impressed by the advantage of intracellular records, in spite of the increased difficulty of this technique.



A comparison of the surface EEG record with the intracellular records from pyramidal cells contributed much to our understanding of the significance of certain waves in the EEG, for example EPSP's with alpha like surface negative recruiting potentials, IPSP's with surface negative slow waves and the wave of the spike and wave complex during "Petit Mal" like epileptiform discharge.[116,117,120,122]

I was also heavily engaged in neurochemical studies with Allan Elliott (Figure 10), Leon Wolfe, and Ikuko Koyama together with some research fellows. We were studying acetylcholine and the amino acids liberated from cerebral cortex during different states of activation, sleep and waking, and during experimental epileptic discharge.[115,119,121,123] I decided to devote my research energies in the future to neurochemical and microelectrode studies of brain activity, and in their combination using the multibarrel microiontophoretic technique.

Decision to Move to the *l'Universite de Montreal*, 1965

The EEG department was doing well under Peter Gloor's guidance and I felt as though I had seen enough EEG records for a time, and would rather explore more thoroughly the mechanisms of brain activity at the cellular and chemical level for the rest of my research career.

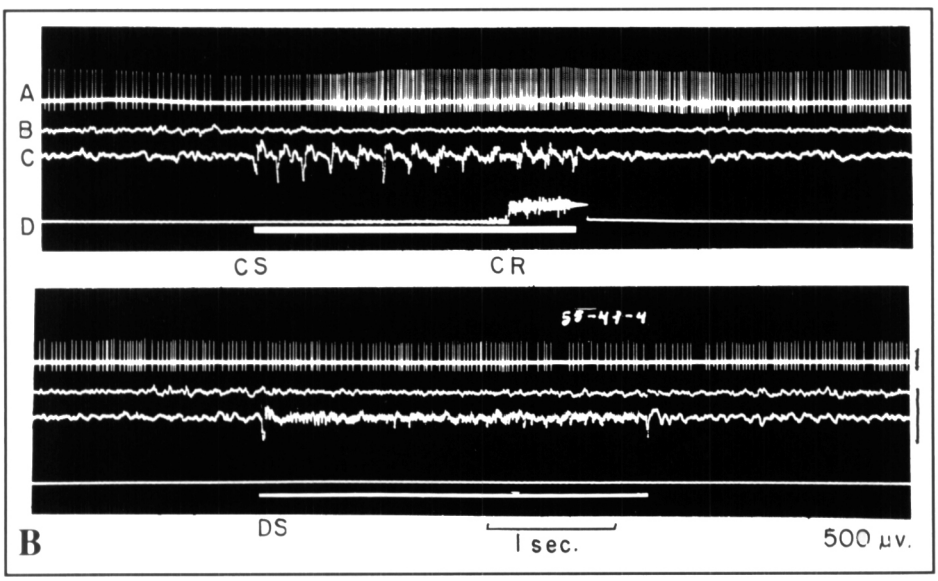


Figure 9 — Chronic Microelectrode Studies; Conditioning in Monkey with G. Ricci and B. Doane. ***A.*** *Monkey in chair with micromanipulator attached to skull and hand attached to switch which is pulled to avoid electric shock.* ***B.*** *Sample record of units from motor cortex during conditioning; top line=units, 2nd line=surface ECG, 3rd line=surface evoked potentials from occipital cortex in response to the conditioning stimulus (CS), 3rd line=EMG and signal of CR, 4th line-signal of CS (see ref. 96). Lower records show lack of response to the same intermittent photic stimulus at a higher frequency, not associated with shock, the differential stimulus (DS).*

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Prompted by serious political difficulties we were having in Quebec at the time, with organized terrorism directed by radical French separatists against the English, and in order to obtain sufficient space and financial support for expansion into these fields of research, I moved to the *Universite de Montreal*. I was invited by Professor Jean Pierre Cordeau to help establish a center for research in the neurosciences in this French University on the other side of Mount Royal from McGill.

We obtained a generous program grant from the Medical Research Council of Canada and much help from Prof. Pierre Bois then dean of the Faculty of Medicine at the *Universite de Montreal*. We were soon able to recruit several good neuroscientists in neuroanatomy, neurochemistry, neuropsychology and neurophysiology which enabled us to establish a strong team within the Department of Physiology in the Faculty of Medicine.

We then established collaborative projects with our colleagues at McGill who also took part in our weekly seminars which served to help defuse some of the antagonism which had been at the bottom of the separatist movement among the French students at the *Universite de Montreal*. We also invited many distinguished visiting lecturers throughout the years.

An annual International Symposium on a topic of current major interest in Neuroscience was established later. Careful editing and publication of these yearly International Symposia has served to establish the *"Centre de Recherche en Sciences Neurologiques"* at the *Universite de Montreal* as an important Canadian research center of international importance and leadership.

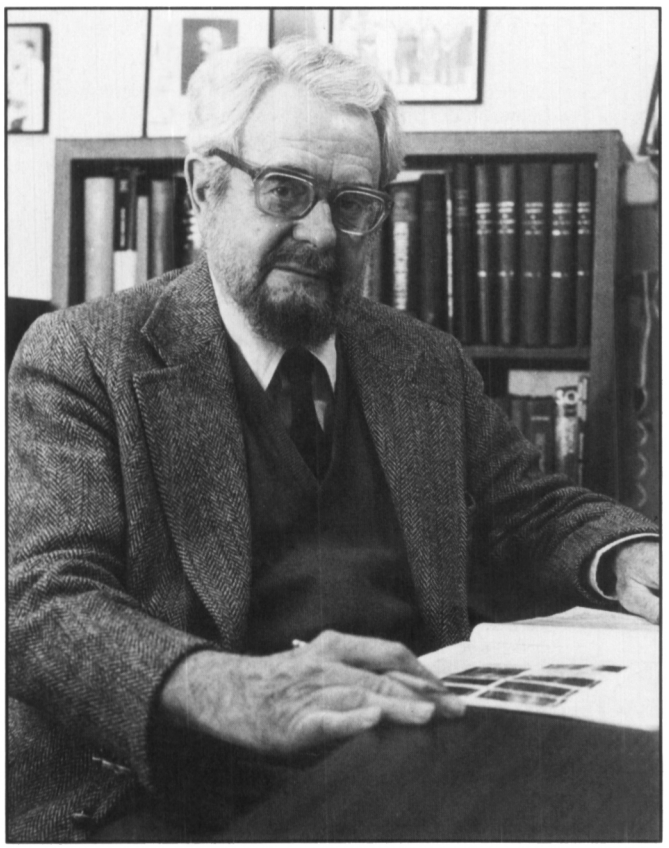

Figure 10 — Dr. K.A.C. Elliott.

Close collaboration with the McGill Neurological Institute has continued, as exemplified by the International Symposium held in my honor in 1970 at Mont Tremblant, organized by Jean Pierre Cordeau and Peter Gloor,[128] and the recent symposium on neurotransmitters organized by McGill University and the *Universite de Montreal* by Avoli, Reader, Dykes, and Gloor to celebrate my 80th birthday in August 1986.[130]

The International Brain Research Organization (IBRO) which we helped to establish in 1960 has recently been reorganized as a Federation of Neuroscience Societies throughout the world, with its Second International Congress held in Budapest in July, 1987. The next International IBRO Congress was held in Montreal in 1991, partly as a tribute to the important role played by Canadians in its conception and early organization.

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Appendix

Historical Introduction, the first 25 years
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