

Notes on the career of Jacqueline Mikol

Jacqueline Mikol

Honorary Emeritus Professor, Université de Paris, France

Address for correspondence:
Jacqueline Mikol · Université de Paris · France
jacqueline.mikol@wanadoo.fr

Additional resources and electronic supplementary material: [supplementary material](#)

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I was born in Neuilly sur Seine in 1936 but my parents lived in Rumaucourt, a small village in the north of France (Pas de Calais). Both were from Jewish Romanian descent, but they met in France. My father was a family physician and my mother, who had interrupted her medical studies before WWII, resumed them after the end of the war when I was at primary school and became a radiologist. During the war, my father was not present at home. He was first a prisoner in Germany, then deported to a concentration camp (Auschwitz-Monowitz/Flossen-burg). Fortunately, he managed to survive and to come back home in 1945 but after this traumatic experience, life would be never easy again. My parents did not want to have any other children. From 1940 to 1945, my mother and I had lived in Beaulieu sur Dordogne, in Corrèze. At the time, as a little girl, I did not realize that our life was in danger and that I was very protected. This gave me some degree of naivety and the feeling, during my first decades, not to be enough prepared to the ups and downs of private and professional life.

In 1956 I got married, then divorced and remarried to François Mikol (1961) who was “Interne”, in the Department of Neurology of Professor Raymond Garcin at Salpêtrière Hospital, when I was “Externe”. I had with François three children, two boys (1962,

1964) and a girl (1970) and later eight grandchildren. My children often criticized me to spend so much time at work. I had to wait for years, when one of them began to do research, to be told that when you begin an experience, you never know exactly when you are going to finish it. My husband, who became a neurologist, was nominated the Head of the Department of Neurology of the Rothschild Foundation in Paris. This gave me the opportunity, after 1980, to frequently collaborate with him till his retirement.

I had been very admiring of my father who resumed his practice, very soon, after coming back from deportation. At the time, a physician took care of medicine treatments, fractures, childbirths, day and night. I was also impressed by the book of Balzac, the Country Physician. So, I decided to study medicine.

I began my medical studies in 1954, in Paris Medicine University, after one year of basic sciences referred to as “Physics, Chemistry and Biology”. I succeeded to become “Externe” (1956), “Interne” of Paris Hospitals (1960) then “Chef de Clinique” in the Clinic of Neurological Diseases in Salpêtrière Hospital (1966-1969). Simultaneously, I was trained in Pathology (Medicine University: 1963-1966) and Histology (Science University: 1966-1967), as I had de-

cided to become a Neuropathologist. Although it seems obvious by now, my training was to investigate the relationships between clinical data and histology to determine the physiopathology of the neurological diseases. Having a dual clinical and biological training was then feasible, which unfortunately, is not the case anymore in France. So, I was qualified as a "Neuropsychiatre" (1968) and had a Research degree in Human Biology (grade Neuropathology-1972). I began my practical training when I was in the Laboratory of the Department of Professor Garcin, writing reports on infarcts, then called softening, and tumors. Claude Vital and Philippe Evrard and later Jean de Recondo were my classmates, under the supervision of Professor Jean Lapresle. I defended my thesis in 1966 on Binswanger's Encephalopathy and related forms, directed by Professor Garcin and Professor Lapresle.

From 1968 to 1983, I became a researcher at INSERM (Institut National de la Santé et de la Recherche Médicale). The Unit was successively directed by Doctor Jean Gruner and Professor Michel Fardeau. During this period, I was responsible for the Laboratory of the "Clinique Neurologique", at Salpêtrière Hospital, Professor Boudin having replaced Pr. Garcin, to perform day-life practice of Neuropathology (1969-1976).

Afterwards, I moved to Groupe Hospitalier Lariboisière-Fernand Widal-Saint-Lazare to set up a Neuropathology Unit (Central Nervous System-Nerve-Muscle), in the Department of Pathology, at the request of Dean Raymond Houdart, neurosurgeon, Professor Bernard Pepin neurologist and Professor Jean Roujeau, pathologist, my former teacher in Faculty. I was alone, in charge, to ensure neuropathology analysis for a long time until 1988 when Doctor Marc Polivka joined me. I was nominated Professor of Pathology in 1985. This was not an easy journey, as a biologist and a woman. During this period, I particularly studied Wilson's disease, for which Professor B. Pepin was a clinical expert and also prion diseases which was part of a national project (Professor J. J. Hauw Project Leader). I coordinated and participated in the writing of a monograph dedicated to CSF. Professor Annie Galian had succeeded to Professor Roujeau. She was specialized in gastro-enterology diseases. She was the one

who encouraged me to study the gut nervous system, which must be included in the training of Neuropathology. After her early retirement, I became Head of the Department, in October 1995.

The first part of my career was mostly focused on science and the second part included some management as well.

During my residencies, two events have impacted my career. Michel Fardeau who was responsible of muscle and nerve biopsies in the Department of Professor Garcin went to the United States for a scientific mission. I was required to learn and to practice the surgical technique till he returns. This triggered my interest in muscle pathology. Reports on ocular myopathies, carnitine deficiency, inclusion myositis, both with Andrew Engel, mitochondrial myopathies... will be published years later. I spent my last stage of "internat" in the Department of Psychiatry, in Versailles Hospital, headed by Professor Serge Brion. Professor Brion was qualified in Neurology, Neuropsychiatry and Neuropathology. He had a critical and insightful mind, a great deal of curiosity and a sense of humor: it was the beginning of a long-lasting collaboration. He was really my Mentor when I developed my research at INSERM, starting from 1968 and beyond. Dementia was the main subject. Serge Brion with Gérard Guiot and Michel Fardeau had developed a syringe-trocar to perform cortical biopsies. At the time, to confirm the diagnosis of dementia, biopsies of cerebral cortex were sometimes prescribed. So, in addition to neuropathological cases, I began to learn transmission electron microscopy. Fortunately, I was helped by technicians, to prepare grids and to operate the Hitachi microscope. In addition, I also had the pleasure and opportunity to work with Jacqueline-Godet-Guillain. I examined the cerebral biopsies of the diseases for which Serge Brion was recognized as an expert for Creutzfeldt-Jakob disease, Pick's and Alzheimer diseases. The research center where I worked had been created by neurologist Professor Garcin, psychiatrist Professor Delay, and biologist Professor Couteaux. The main aim of this research lab was to gather researchers from different disciplines to together collaborate. Pathophysiology of neuro-muscular diseases were one of the main topics of the group. The Center was located at Pavillon Risler, a very old



Figure 1. Meetings of the French Society of Neuropathology in Tunis.

Upper part (from left to right):

First row: J. Gautron is 1st, P. Dreyfus is 3rd, A. Rouche is 4th, the author is 5th, M. Paturneau-Jouas is 6th, M. Tommasi is 7th, M. M. Berard-Badier (blue umbrella) is 8th.

Second row: M. Pluot is 1st, M. Chevalley is 2nd, F. Tomé is 3rd, R. Escourolle is 4th, J. F. Pellissier is 5th, M. Baudrimont is 6th, P. Gaspard is 7th, C. Duyckaerts is 8th.

Background: J. F. Foncin (pink umbrella) is 1st, J. C. Turpin is 5th, N. Baumann is 6th, A. Privat is 7th, J. J. Hauw is 8th.

Lower part:

First row: M. Ben Hamida is 1st, his wife C. Forestier is 2nd, J. Flamand is 3rd, C. Duyckaerts is 4th, M. Baudrimont is 5th, O. Robain is 6th, F. Dubas is 7th, M. M. Rouchoux is 10th, M. Coquet is 11th. D. Henin is sitting in front in the middle.

Second row: M. B. Delisle is 3rd, F. Chapon is 4th, J. Lapresle is 6th, C. Vedrenne is 7th, M. Pluot is 9th, the author is 10th.

building in Hopital de la Salpêtrière. The biologists were working on the neuro-muscular junctions of the torpedo fish. The aquarium was always an object of fascination for one of my children when he or she came with me to the laboratory. When the first “open laboratory days” took place (1968), organized by Bernard Barataud, the President of the “Myopathic Association” and Michel Fardeau, the biologists decided that, as a medical doctor, I had to welcome visitors to whom unfortunately we had very little to show that could have a concrete impact on quality of life of patients. This was the first “Telethon”. My work was complemented by an experimental and neuropathological study of the connections of the latero-dorsal (LD) nucleus of the thalamus and its relationships with the limbic system. I began to study twelve anatomo-clinical cases of vascular origin in man. Serge Brion had noted that in some cases of memory disturbances, not only the hippocampomammillo-thalamo-cingular network was involved but the LD was also modified. The experimental study was performed in non-human primates in the laboratory of Robert Naquet in Gif sur Yvette. It was shown that the LD is part of a large parieto-cingulo-parahippocampic network with multiple direct and reciprocal connections. Advice was provided by Professor HGJM Kuypers, who asked me to come to Amsterdam, to discuss the report I had sent to Brain Pathology. I was very grateful to him. The studies of the limbic studies had shown the prevalence of the lesions of the LD, over those of the dorso-median nucleus of the thalamus. These results were the object of a controversy upon the hypothesis of Victor and Adams. They were at the origin of anatomical reports on memory disturbances and the relationships between memory and hemispheric functional specialization. It should be noted that these studies were performed before the practice of functional MRI which since have shown more complex networks.

I also studied tissue cultures of nervous system, made in Maximow slides, to study aging and consequences of extracts of pathological specimens of cortex but survival was too short.

Professor Brion sent me to the meeting of the American Association of Alzheimer’s disease, created by families and chaired by Princess Yasmina,

daughter of Rita Hayworth. The Committee suggested to create the same type of association in France. As I was not any more a clinician, I proposed to Professor Françoise Forette to create and to chair such an association with a scientific comity. I will remain in the committee of France Alzheimer for many years.

I was in charge of the Diploma of Normal and Pathological Aging (1997-2003). Before, I had been in charge of the certificate of “Master” of Pathology (Paris University).

I was elected member of the French Society of Neuropathology. Founded as a Club in 1964 (Madeleine Bérard-Badié, Sege Brion, Raymond Escourolle, Edith Farkas, Jean François Foncin, Jean Gruner, Jean Lapresle, Gilles Lyon, Maurice Toga, Michel Tommasi), it became a scientific Society in 1989. I chaired the Society from 1990 to 1992. The meetings of the French Society, before the pandemic, took place either in Paris in winter or in another city in spring, with international participation or as joint meetings with our European Colleagues or extra-European Colleagues, especially from Canada. These meetings have created productive relationships between members of the Society and allow to enjoy social life together.

I have participated to Concerted Actions on AIDS chaired by Professor Françoise Gray and Prion Human Diseases, chaired by Professor Herbert Budka. I would like to emphasize the importance of these Concerted Actions. They were the source of scientific progress and collaborative research. Each of us strived to show new results. Many reports and books were later published, many friendships took place and strong links were established between Neuropathologists. Each meeting was in a nice location and enabled to socialize in a very pleasant environment.

I shall say the same for congresses and conferences. Nowadays, for different reasons accelerated by COVID-19 pandemic, most meetings are organized with a computer and internet systems. It is difficult to be satisfied by an Orwellian evolution of Neuropathology. I had the pleasure to see and to listen to the main famous colleagues, to participate in poster sessions extremely rewarding and stimulat-



Figure 2. HIV Concerted Action, Cork, Ireland.

First row (from left to right): K. Majtényi is 2nd, the author is 3rd, F. Gray is 4th, K. Keohane is 5th, I. Elovaara is 6th.

Second row: J. Artigas is 1st, F. Scaravilli is 3rd, P. Liberski is 4th, F. Razavi is 6th.

Third row: P. Trotot is 1st, F. Morinet is 2nd, D. Boche is 4th, J. Bell is 6th.

Last row: R. Gherardi is 1st, H. Goebel is 2nd, A. Aguzzi is 5th, H. Budka is 6th.

ing. Furthermore, to become a member of Neuropathological Societies, it was necessary to present at least twice. To illustrate the spirit of this community combining scientific excellence and ability to enjoy life, I shall tell a short story. As the International Congress was taking place in Perth, chaired by Professor Byron Kakulas, I naively asked to Professor Colin Masters, one of the organizers, if Bali was far from Australia. The answer was “about 2 hours of flight!” Inspired by the question he followed up with “Great idea! Let us organize a small pre-meeting in Bali focused on Brain Tumors and Alzheimer’s Disease, from Neuropathology to Molecular Biology”. This enabled us to go deep into some specific scientific subjects and provided a unique opportunity to visit

Indonesia and to discover Borobodur temple at sunrise and Bali Island. Our small group of French Lady Neuropathologists (M. Baudrimont, C. Dumas, M. N. Delisle, C. Lacroix and myself) had Herbert Budka as improvised volunteer bodyguard.

In April 1991, delegates from the National Neuropathological Societies of the European Community met in Paris as the future existence of Neuropathology in Europe appeared compromised. I had proposed that the meeting took place in my department as Paris was easily accessible from different countries. The delegates were the following: Professor Dr. H. H. Goebel, Professor Dr. W. Schlote, Professor Dr. W. Wechsler (Germany), Professor R. Cotrufo, Professor N. Rizzuto, Professor D. Schiffer (Italy), Dr. D. Troost (The Netherlands), Professor D. I.

Graham, Dr. Janice R. Anderson, Professor R. O. Weller (United Kingdom), Professor F. Gray, Professor J. J. Hauw, Professor J. F. Pelissier (France); Dr. S. J. Balogiannis (Greece) had apologized. Professor David Graham chaired this first session and asked a representative from each National Society to give an account of the practice and status of Neuropathology in their country, including training, examinations and accreditation. That was pivotal for the future creation of Euro-CNS.

In 1992 David Graham was appointed as the representative and the chairman of our group. He went to Brussels and obtained to have a representation on the Board of Pathology. Our small group worked a lot and met with other members of the European Community who had become EU (European Union) and EFTA countries (European Free Trade Association) including Austria, Finland and Switzerland. The Confederation of the Neuropathological Societies or EURO-CNS, term proposed by Roy Weller, was established in June 1993, including delegates and deputies. A constitution of EURO-CNS was written by David Graham and Janice Anderson in 1993 and multiple sessions involved the research inventory, the rules of training and examination, the clinical practice. A logo was created. In 1994, David Graham was elected President of EURO-CNS to whom I succeeded, when I was organizing the Vth Congress of Neuropathology in Paris, under the auspices, for the first time, of EURO-CNS. To summarize a long process, in March 1997, there was an official recognition of the subspecialty of Neuropathology by the Management Council of UEMS (Union Européenne des Médecins spécialistes). It needed to be reactivated in 2003 but was rejected in 2004. In 2005, the European Parliament voted that recognition must comply with the 2/5 rule, that is in 10 countries out of 25 (25 at the time). We finally never succeeded to obtain the extension of the recognition of neuropathology at European level and it only continued at a national level when previously established. We probably should have had more support from our clinical colleagues. Details were reported in an overview on Neuropathology in Europe (2006). I would like to pay tribute to Dirk Troost for his instrumental role in the organization of exams and courses as well as Hans Goebel and to Ilja Huang, the essential EURO-CNS secretary.

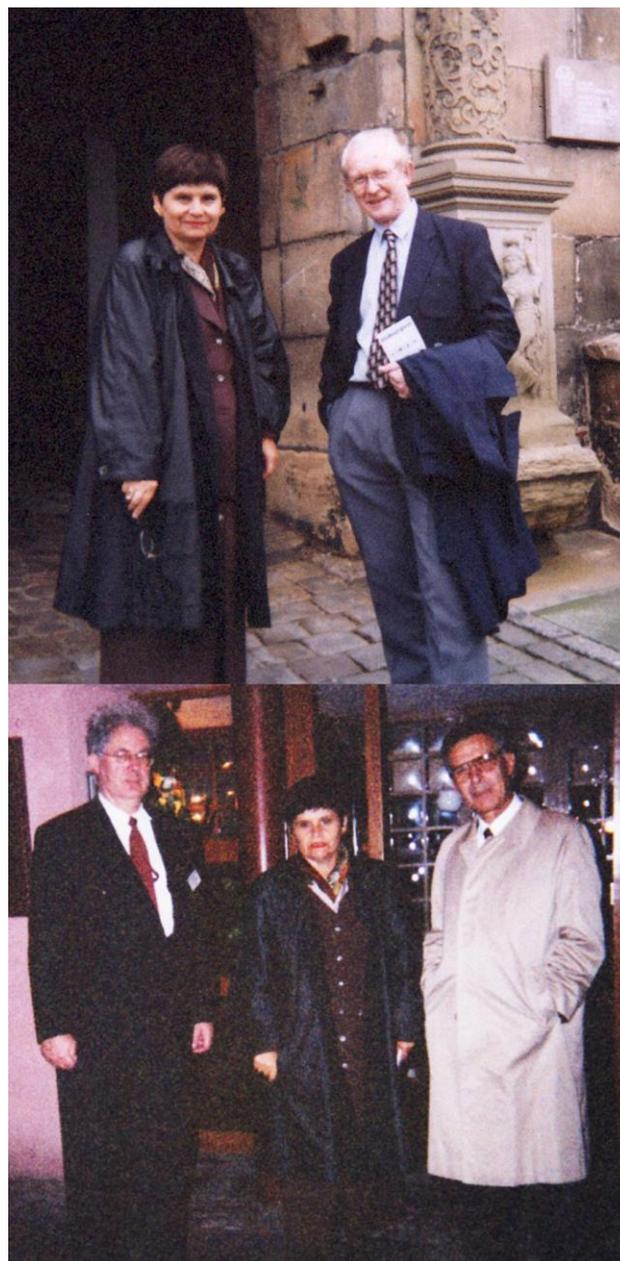


Figure 3. Euro-CNS Meeting.

Upper part: The author and D. Graham

Lower part (from left to right): H. Goebel is 1st, the author is 2nd, N. Rizzuto is 3rd.

Nowadays, Neuropathology is recognized only in a few countries but EURO-CNS is still active, organizes courses and examinations, and patronizes every four years the European Congress whose abstracts are published in *Clinical Neuropathology*.



Figure 4. European Meeting of Neuropathology.

Upper part (from left to right): P. Kleihues is 1st, the author is 2nd, J. Artigas is 3rd, G. Gosztanyi is 4th.

Lower part: the author is 1st, Roy Weller is 2nd, F. Gray is 3rd.

After my retirement, daily life was not easy. Suddenly my timetable had changed. I am not exactly a housewife having been so active professionally. I went to Romania with Professor H. Goebel to teach Neuropathology, invited by Professor M. Alexianu, under the auspices of EURO-CNS. I started the inventory of the slides of the Dejerine Foundation, which led me to publish historical reports about this Foundation, the life of Augusta Dejerine-Klumpke, the original slides of facioscapulohumeral myopathy and Dejerine-Roussy syndrome. I have updated the history of Pick's disease.

Fortunately, Dr. J. P. Deslys, Director of the NeuroPrion Sepia Unit, François Jacob Institute, at

CEA proposed to join his group to study experimental prion diseases. I was back to the lab! He wished to have someone with a clinical and experimental experience. Thus, I have a very constructive exchange with the members of the team, biochemists, veterinarians, research engineers, technicians, of very different backgrounds and ages from mine. These fruitful intergenerational confrontation of concepts with a wide range of extremely diverse experiences gave me the opportunity to better understand the strains, the transmissions and to publish, recently a paper which, I believe, provides some compelling data to outstanding questions.



Figure 5. Department of Pathology Hôpital Lariboisière Paris. The author is in the middle of the front row and M. Polivka is in the last row, the 5th from left to right.

I feel you cannot do this job if you are not fully engaged in the research. I had the privilege to practice neuropathology at a golden age when there were too many silos. I believe it would be difficult for me to focus exclusively on a specific disease like oncology, although I have studied a lot of glial tumors, lymphomas, pituitary adenomas now almost exclusively dependent on molecular biology. I had chosen Serge Brion as a Mentor because he was not always looking for what was exactly in mainstream thinking. Having a deep understanding of the existing knowledge is key but combining different disciplines with new way of thinking often enables to address challenging unresolved biomedical issues and go to the next level. Moreover, even if the incents of administration promote overconcentration between hospitals, it is also necessary to avoid any situation of monopoly which leads to a single thought whereas diversity is always a factor of progress.

Next September, I shall be 85 years old. From my internship until now, I have been practicing Neuropathology in a Life Science laboratory, which I feel a real gift and has brought me a lot of happiness.



References

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