

# From Parma to Pisa: building a great physiological institute

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## ABSTRACT

*This is a remembrance of the early stages in the development of Giuseppe Moruzzi's school at the University of Parma in the years immediately following the end of the second World War, and its subsequent move to the University of Pisa with the foundation and growth of the Pisa Institute of Physiology, and the great contributions to neurosciences with the studies on the brain stem reticular formation and sleep physiology.*

### **Key words**

*Brain stem reticular formation • Cerebellum • Midpontine preparation • Sleep*

I would like to start by thanking my friends, all well-known disciples of Professor Moruzzi, for having asked me to participate in this commemoration of our Mentor on the occasion of the celebration of the first centenary of his birth, here in the Institute he directed for more than 30 years, and made famous worldwide. You may certainly ask yourselves why I have been invited, since I was associated with Professor Moruzzi more than fifty years ago, I have been a neurophysiologist for slightly more than ten years, and I am rather a clinician by profession and an amateur as a physiologist; an amateur but perhaps not entirely faithless.

My participation, which honours me greatly, has been requested I think, because the adventure, the fascinating history of the Moruzzi school starts from Parma, and, after the regrettable loss of Arnaldo (Momi) Arduini, I am the only disciple who can commemorate those years of beginning. *Commemorating* means remembering together, and *commemoration* sounds something like *commotion*. In this case commemorating implies talking – in a somewhat immodest way – talking about ourselves,

remembering our own youth. However, any translation is deceiving, and remembering means translating what we were in those past years of our life with the sight and the words we have and can use today. We have to start from Parma, the city where I was born, where I spent the first part of my life, where I attended Medical School soon after the end of the Second World War. Parma has the peculiar history of having been for several centuries the capital of a small state, which remained independent until 150 years ago. As a capital Parma enjoyed and suffered court life, had very strong links with French culture (in the second half of the eighteenth centuries Parma was the second city after Paris where more copies of the *Encyclopédie* were read), Parma still embodies the wise idleness of provincial life and the vitality of cosmopolitan cities, combines the gossip about our neighbours' affairs with the intellectual curiosity for the happenings of the greater theatre of the world, *el gran teatro del mundo*. We must not forget what was the historical period in which I first met Professor Moruzzi in Parma. World War II had finished, and everybody, but young people in particular, ardently

wished to leave behind themselves the sad remnants of a recent past, and longed with enthusiasm – sometimes a childish enthusiasm like that of Fabrizio Del Dongo on the Waterloo battlefield – for the intellectual freedom promised by the new times.

Certainly, in 1945 the cultural background of a young man in Parma did not prepare him to the challenges of a scientific career: in my case classical studies and a family atmosphere influenced by my father who was a man of letters and had a sculptor as grandfather, and my mother who had a degree in French literature, in a home where the long evenings without television were enlivened by conversation about books, art, and by the real passion of people in Parma, opera singing. When, during my second year at Medical School, I do not remember why (but, as you know, decisions having the most lasting effects are commonly taken on the basis of feelings not destined to last), I entered as a research student the Institute of Physiology, I think I would not have developed a new vocation for scientific research (true vocations are rarely inborn, they require occasions, atmospheres, education, luck), if I had not met, rather than a mere *scientist*, a *person* like Giuseppe Moruzzi, who had just come back as Professore Incaricato (Temporary Professor) to the university where he had graduated, after his scientific adventures in Brussels with Frédéric Bremer and at Cambridge with Lord Adrian, Nobel Laureate. At that time, I was not certainly in the condition to appreciate Moruzzi's extraordinary scientific value, but I was immediately attracted by his mobile intelligence, his wide cultural interests also in the field of humanities, his cosmopolitan experiences in the mythical universities of North Europe (in 1945, a boy like me living in Parma had once visited Milan, had once seen Venice and had climbed a few times to Urbino during the long summer holidays with his family on the beaches of the Adriatic coast). Raised as I had been by my mother's strict religious spirit, with some jansenistic rigour inspired by assiduous readings of the great French moral writers of the seventeenth century, I was strongly impressed by Moruzzi's intellectual rigour, scientific honesty, ethical vision of research. Perhaps, not enough has been said of this aspect of Moruzzi's, but in times such as ours, dominated as they are by a faster and faster, hurrier and hurrier pace of research, by publication obsession, and – for good and bad – striving

for impact factor, the recommendation transmitted by Moruzzi to his disciples, and by us to our own disciples, should not sound unvain: after writing a manuscript replace it into the drawer for a few days, and then read it again as if it were not yours, read it with the sight of a reviewer; do not sell hypotheses as evidence, do not consider evidence as good for ever. The motto "*ne varietur*" (not to be changed) is not part of the scientific dictionary.

It is long time since I have not entered again the Institute of Physiology in Parma, which I have no doubt has been radically changed during the many years it was brilliantly headed by Arduini, first, and then by Rizzolatti. Therefore, I can better remember, or recreate in my memory, how it was at the time of my *Lehrjahre*, my years of apprenticeship. I have the most vivid memory of the long narrow room, heated by an earthen stove (central heating was off because we were still suffering from the disasters of the war), the room where almost all research activities were concentrated; where, on one side, Professor Moruzzi and Arduini were stimulating the cerebellum in a thalamic cat, and, on the opposite corner, I was playing with stimulation of the optic lobes of a pigeon. And whenever I happen to consult – not frequently any longer – my curriculum, I live anew the emotion I felt when, after less than one year of research work Professor Moruzzi generously told me to make personally a short presentation at a meeting of the Italian Society of Experimental Biology, a paper that is still the first one in my list of publications, dated December 1946; an unexpected reward for an unexperienced young man only 20 years old.

I also remember how the Institute was filled up in the afternoons by the irresistible exuberance of Cesare Bartorelli, one of the dearest friends and colleagues of Moruzzi, who used to divide his time between clinical activities in the Department of Medical Pathology on the mornings, and research activities in the Institute of Physiology on the afternoons. Cesare Bartorelli later became my second Mentor, the one who taught me how to be a medical doctor, who introduced me into the secrets of arterial hypertension.

We still had to record on smoked drums (smoking recording drums was the first technique I learned in the laboratory), because we had almost no funds available. However, we did not feel this was a great limitation, being all taken by the enthusiasm, by the feeling that we were anyway tackling problems

along the paths set by the famous international investigators Professor Moruzzi had been working with. The success of some of the work performed in those years, despite the limitations in technical means, has taught me that enthusiasm and originality of thought can overcome lack of funds and technical sophistication, and lead to scientific results of great interest and importance, as happened to Moruzzi, who in those years completed innovative research on the physiology of the cerebellum and experimental epilepsy. Nonetheless, I still remember with some emotion the day electronics first entered the laboratory under the aspect of a bulk, home-made square-wave stimulator to replace an old fashioned (dated 1890) DuBois Reymond faradic stimulator I had been working with until that time. The new electronic stimulator was the one I subsequently used to prepare my MD thesis and by which I did several of my early publications.

Then did the Pisa years come. Giuseppe Moruzzi, on his return from the Northwestern University in Chicago, where he had worked as Visiting Professor with Magoun and Brookhart, and carried out the memorable experiments on cortical activation by the brain stem reticular formation, was called in 1949 to the chair of physiology at the University of Pisa, and thus to the task of heading a large and famous institute, which had previously been headed by Aducco and Spadolini, and which was to be supported financially by enlightened grants of the Rockefeller Foundation and the European Scientific Office of the US Air Force.

I joined Moruzzi in Pisa soon after I graduated as an MD in Parma, in the second half of 1950. In a brief address I gave in 1980 on the occasion of the IBRO symposium honouring Professor Moruzzi on his seventieth birthday, I remembered the 1950s in Pisa as a “magic period”, that of “the infancy of Moruzzi’s school”, and – needless to say – infancy has a spell of magic in it, especially for someone who is no longer young. These were the years when modern neurophysiology was borne in Pisa, and other fields of the neurological and medical sciences were also fertilized, as testified by the presence in Pisa during the 1950s of a neurosurgeon such as GianFranco Rossi and neurologists such as Hrayr Terzian and Mario Parma. Though many of us have stopped cultivating neurophysiology, you will pardon us if we presume to have some little share

of merit for the wonderful achievements that were obtained here in Pisa during those years and subsequently by Moruzzi’s disciples who have remained neurophysiologists and have continued illustrating neurophysiology. Most of them are here today, and I feel dispensed to name any of them, except for those who can no longer be with us, Arduini and Pompeiano.

These were important and exciting years of our life. International horizons started being opened to ourselves, young men coming from provincial towns as we were; invitations to present at meetings abroad, rare and deeply appreciated at that time, were beginning to be addressed to us; fellows from various parts of Europe and the United States were flowing into the Pisa laboratory to work “under Moruzzi”, thus giving us some opportunity to exercise our uncertain and bookish English. Then the time came for us to go and work abroad. It was in 1953 when I left Pisa to work in the United States with John Brookhart thanks to a fellowship of the Rockefeller Foundation. After almost sixty year it is not easy to understand what meant to a young investigator in those far years, and perhaps to a young man *tout court*, to disembark to the United States. It was truly a disembarkment, since in those days the cheapest way of travelling to America was by boat, sailing for nine days from Genova to New York harbour. In the early nineteen fifties, America was a myth in the imagination of a young man from Italy; a myth created and cultivated by Hollywood comedies, and readings of the “Americana” anthology by Vittorini. I feel the renovation of Italian university research owes something to our generation, the so-called “Americans”, the small group of those who had worked in the States during the 1950s, and whose contribution represents – I feel – one of the most positive and lasting aspects of the 68 revolution.

The atmosphere at the Institute in those years was exciting, happy, friendly and familiar. However, it would be wrong thinking it was democratic. We were indeed in great familiarity with our teacher and his family, that lived in the upper floor of the Institute, while the penniless disciples lived at the ground floor in small unheated quarters, which were connected to central heating only when they were subsequently nobilitated as laboratories. Nonetheless, no one of us would have dared to consider Moruzzi as *a primus inter pares*, the first

one among peers. Rather, we may have considered him as a *pater familias*, an enlightened prince, as the Grand Duke Pietro Leopoldo, whose marble statue looked at us with benevolent eyes whenever we crossed Piazza Santa Caterina, the large green square on our way to and from the Institute.

As far as science was concerned, the first years in Pisa were unavoidably dominated by the development of the innovative experiments done by Moruzzi in association with Magoun: after one full century during which neuroscience had been intrigued, perhaps obsessed, by the research of “specificity”, the specific functions to attribute to any minute brain area, to any group of neurons, the sudden breath of the new conception of a general brain activating system, of sleep as a mere cessation of the state of wakefulness, was producing enthusiasm and energies difficult to be described, in all of us.

However, science cannot progress by enthusiasm alone, unless enthusiasm is coupled with rigour and criticism, and with faith in the ethics of scientific truth. This is probably the most important lesson I have received from Giuseppe Moruzzi, or at least that for which I am most grateful to his memory. I well remember when in 1956 GianFranco Rossi, Mario Palestini, Cesira Batini and I began the experiments with progressively more and more caudal transections of the cat brain stem in order to find out at what level of the reticular formation a transaction turned the electroencephalographic and behavioural pattern of continuous sleep of Bremer’s *cerveau isolé* preparation into the alternating sleep and wakefulness pattern of the *encéphale isolé* preparation. There were no automatic recording systems at that time, and, being a kind of nocturnal animal, I passed many hours watching at the experimental cat’s electroencephalogram. When we got to produce that brain stem transaction that we subsequently called “*midpontine*” in an article published in *Science*, I remember I continued to wait for several hours and in vain the periodic appearance of the electroencephalographic pattern of sleep. Against our expectations, moving the section caudally by 2-3 mm, rather than substituting the pattern of permanent sleep of the *cerveau isolé* preparation with the physiological pattern of sleep and wakefulness alternations, regularly produced an opposite pattern of uninterrupted wakefulness. Once we could repeat this observation in several animals,

I mounted the steps leading to Moruzzi’s office with a good deal of anxiety, bringing with me, together with heavy packages of electroencephalograms, the worried awareness that our observations in the midpontine cat pointed to the presence in the caudal brain stem of neuronal structures capable of actively inducing sleep: obviously, an interpretation of sleep quite different from that – sleep only as absence of wakefulness – which had been derived from Moruzzi and Magoun’s experiments on the ascending reticular formation. Moruzzi’s reaction can be taken as a model of scientific rigour: hypotheses stem from observations, and new observations can and should modify hypotheses. Moruzzi often cited Claude Bernard: experiments are performed *pour voir*, and what really matters is what has been seen. Thus, a finding that other investigators would have taken as a refutation and an offence, turned to be the source of a novel important area of research. Not for nothing, in his parting words at the end of the 1980 symposium, Professor Moruzzi cited Blaise Pascal’s admonition: *travaillons donc a bien penser*, let’s work in order to think clearly.

It is not up to me, deserter from neurophysiology, illustrating what has been the contribution of Moruzzi to the neurosciences and I know this has been illustrated very well during the various days of this conference. I also had the occasion, a few years ago here in Pisa, to comment what Moruzzi’s teaching has meant to those of us who have subsequently become clinicians. During more than 50 years since I left Pisa, scientific research and, in particular, neurophysiological research have obviously changed and to a very large extent. Technical progress and advances in the understanding of brain functioning have been multiple, important and indisputable. Therefore, it should not sound as the complaint of a *laudator temporis acti*, a commender of the past, if I indulge to remember some of the pleasures of research that perhaps have gone lost nowadays: research protocols not rigidly prefixed; the pleasure of the unexpected observation under our direct sight rather than coming from the statistics of the computer; the preminence of seeing over foreseeing, of vision over prevision; the lack of jealousy and suspicion in exchanging information between investigators, the freedom from the obsession about the impact factor (publishing on the *Journal of Physiology* or the *Archives Internationales de Physiologie* or

*Journal of Neurophysiology* was longed for because these were the journals where Sherrington, Adrian, Bremer and Magoun had published), the thought of patenting the results of our research would never come to our mind, and would have appeared to us an unforgettable offence to scientific freedom. And so it still appears to me nowadays. Many of these pleasures have been lost today, or at least have become difficult to enjoy, perhaps because the fields of science have been ploughed quite deeply, and are now tilled by agriculturists rather than the humble farmers of the low lands along the Po river.

What has been left today of what we did then with such a great enthusiasm, and – let me say – with such a great success? More than a question it is perhaps a *péché de vieillesse*, a sin of an old man. Today the success of a publication is measured quantitatively by the number of citations, but, hélas, electronic memory is strong but short, and only citations after 1996 are noted by specialized web sites. Computer memory, wide but short, is an unfaithful instrument that cannot measure that continuous

flow of knowledge, that subtle heritage often hidden in publications and understated in the restraint of human relations, which weaves the threads of the history of science. The beginning of the first of T.S. Eliot's Four Quartets comes to my mind:

*Time present and time past  
Are both perhaps present in time future,  
And time future contained in time past.*

In the obituary of Giuseppe Moruzzi published on *Archives Italiennes de Biologie*, Ottavio Pompeiano, whom we have also lost in the meanwhile, describe with moving accents Giuseppe Moruzzi in the last months of his life, conscious of the rapid aggravation of his illness, gathering his personal books from the Institute study to send them back home, not forgetful of the old wisdom of the seventeenth century French moralists: *mettre quelque temps entre la vie et la mort*, to let some time between life and death. This is perhaps the last and most important lesson we should learn from our Teacher.