

French Neuroscience and its relation to industry

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Current debates on the applications of science are generally seen as little relevant to the field of neuroscience during its first decades of development (1950-1970). If neuropharmacology is excluded, specific characteristics of neuroscience generally prevented the rise of large scale technological innovation and broad industrial developments, both understood as a result and as a means for fundamental research, or as a converging domain between scientific discoveries and technological applications. Neuroscience first developed as field based on local and rather small laboratories, in a manner close to the experience of Claude Bernard's school in France in the XIXth C., and contrary to the emergence of a Big science, as Nobel Prize winner, John C. Eccles still acknowledged in 1973¹.

This does not imply that the enterprise of neuroscience appeared aside from the great improvements of biology and their intricate relations with industry. Neurology, neurophysiology and neuroanatomy, and then neuroscience, developed or adapted numerous instruments and techniques subject to processes of industrialisation. These disciplines benefited from technological progress, especially from technologies arising after the Second World War such as electron microscopy or ultracentrifugation. However, until recently, the schemes of industrialisation of many biological domains, including in a few cases the neurobiological sciences², did not yield great and fundamental successes in neuroscience compared to those acquired with local processes of building and improving scientific instruments and methods within small research groups, as still was the case with the new patch clamp technique by Nobel Prize winners (1991), Bert Sakmann and Erwin Neher, based on the building of a high impedance electronic amplifier.

¹ John C. Eccles The Discipline of Science with Special Reference to the Neurosciences, *Daedalus*, 102, Special issue, *The Search for Knowledge*, 1973, 85-99, p. 85-86, 93. « I will of course be looking at the subject of research from a very different standpoint from that of big physics. Fortunately nothing in biology is yet comparable with the situation in physics, and most biological research is still carried out under conditions which would have been usual for physics until the 1940's. Most efforts to build biology up into something equivalent to large scale physics seem to me to have been disappointing and I think misguided. I believe that in biology we are still in the enviable position of being able to work as creative individuals with, of course, small teams blending those special talents that are required in technical and theoretical attacks on fundamental problems [...] As I have observed the main developments in neurobiology, I have come to see that we are still in a stage where the imaginative ideas of individuals play a leading role and that large programs of scientific research are often opportunistic [...] In my experience the best sized group is two to four people. These can fit into one research room and actively participate in the experiment in hand. All can watch the results and talk about their meaning and what to do next because, as I see it, biological research is still a kind of warfare against the unknown ».

² For example, the discovery of neuropeptides by Nobel Prize winner, Roger Guillemin, requiring specific extraction procedures of peptides from large amounts of biological material.

In neuroscience, objects under study are usually poorly applicable to patent deposits. However, the specific traits of neuroscience show that if relations with industry were less important than in other fields, they were nevertheless pivotal in the last decades. Our analysis shows that these relations do not generally follow a linear scheme from scientific discovery to industrial application, but they create trading zones which are beneficial to new emerging scientific and technological fields.

In the second half of the nineteenth century, a number of instruments were invented and introduced by physicists and physiologists, especially in the field of physiology, and particularly in muscle and nervous physiology. These tools revolutionised the disciplines which used them, but also their objects. A new instrumental physiology emerged³, with the study of muscle and nervous electrical activities and the objectivization of the latter by the former. Modern physiological instruments not only belong to neurophysiology, which appeared in the twenties, but also to the clinics, as respiratory medicine or neuroendocrinology. However, many of these instruments derived from those of neuromuscular physiology⁴, in close connection with the objects and the methods of neurophysiology.

The making of such instruments usually began with the manufacture of prototypes by scientific themselves and their technicians. Rapidly, scientific commissions and institutes appeared for their standardization and diffusion, such as the *Institut Marey* hosting a commission devoted to the control of graphical instruments used in physiology. Étienne Jules Marey was a productive instrument maker collaborating with the famous royal clockmaker family of Antoine-Louis Breguet and Charles Verdin, in the manufacture and the marketing of his technological inventions.

This golden age of instrumentation can be seen in similar manners in all parts of the industry of precision instruments, with the opening of international institutes and close relations established between scientists and manufacturers, the formers in search of technological improvements and the latter following the desires of ever changing scientific fields⁵. For nervous physiology, this period of mechanical instrumentation was based on up to date manufacture abilities until the twentieth century. The *ingénieur des Ponts et Chaussées*, Georges Weiss and Louis Lapicque, professor of physiology at the Sorbonne, continued this tradition in Paris, in collaboration with the instrument maker Boulitte (Paris), later merging his company with Verdin. However, unlike Keith Lucas in Cambridge, French physiologists were not directly involved in the marketing of their new instruments. Public research and private business were largely separated in France. On the contrary, Lucas, professor of physiology in Cambridge, was also involved in a private company. He was one of the directors of the *Cambridge Scientific Instrument Company* (CSI) selling the instruments he devised.

³ M. Borell. Instrumentation and the rise of modern physiology, *Science and technology studies*, 1987, 5, 53-62.

⁴ For example, the French *capsule de Marey* and *rhéotome répétiteur*.

⁵ The Precision Makers: a history of the instrument industry in Britain. Mari E.W. Williams ed., Routledge, 1993, London.

Most mechanical instruments devoted to physiology remained highly specialized and were not widely distributed in the twentieth century. In the field of neurology and neurophysiology, the stereotaxic instrument was an exception when surgeons could design an instrument for human neurosurgery⁶. It was made up of a steel framework positioned on the head of the patient. It allowed to direct electrodes within specific regions inside the brain through a trepanation aperture, using a coordinate system. The device was widely used for deep brain stimulations and for the destruction of inner localised tumours⁷. The revival of this mechanical device occurred after 1945, when its clinical use was fully accepted. Several French physicians and scientists were involved in the French part of the story. Paul Dell, Antoine Rémond⁸, Henri Gastaut, Robert Naquet, all contributed to introduce the stereotaxic instrument in France, then used in the United States for fundamental research. The idea and the first attempts to manufacture such device go back to the laboratory of Karl Ludwig with Dittmar in 1873. Only after 1908, did Robert Henry Clarke and Victor Horsley build and use a stereotaxic frame on a monkey. Clarke himself tried to adapt it to man. First convincing attempts were made by Kirschner in 1933 and then by Spiegel and Wycis in 1946. Since then, the idea of the marketing of the instrument was evident. It was necessary to choose the best coordinate system which would be most appropriate to obtain reproducible results in man. The industrial production of a stereotaxic device was launched by the Sweden Lars Leksell from Stockholm. He used an arc-quadrant system in 1949 and founded the Elektra company in 1972. Elektra patented the gamma knife in the eighties. In France, the neurosurgeon Jean Talairach from Sainte-Anne hospital devised his own coordinate system the same year independently. This system allowed making measurements of deep structures with direct and indirect radiographic data. It was commercialised by Dixi company. However, Talairach was not directly involved in the industrial making and marketing of the instruments.

Paul Dell, from Henri-Rousselle hospital (Paris) brought back the instrument which H. Magoun had devised at UCLA. Dell manufactured his own instrument, with some improvement, and worked on the industrial manufacturing with the company *La Précision cinématographiques* (France, Asnières). Antoine Rémond, from Salpêtrière hospital, with his uncle Alphonse Baudouin and his colleague Houdart, attempted to improve the instrument with the company ECEM⁹. He used CNRS funds for this research. Plans were made by professional industrial designers and a prototype was manufactured. However, Rémond did not commercialise his instrument. After Marey's technological innovations, French neurophysiology was unable to pursue the tradition, perhaps due to the weakening of French industry. The companies manufacturing and marketing specialised materials remained local.

The same occurred with electrical and electronic neurophysiological devices manufactured manually in France and Great-Britain until the sixties and seventies. Oscillographs (non cathodic) and capillary electrometers were used in self made set ups, with

⁶ J.G. Barbara, 2018, « Localiser les enregistrements et les stimulations électriques du cerveau par la stéréotaxie », *Bulletin de la Shesvie*, 25, 2018, 169-186.

⁷ C. Chéricti, Barbara J.G., 2007, « EEG, trois lettres pour percer les mystères du cerveau », *La revue pour l'Histoire du CNRS*, 19, 21-25.

⁸ *Ibid.*

⁹ *Ibid.*

self made differential amplifiers¹⁰, sometimes built with electronic components given abroad by colleagues¹¹.

In Paris, Antoine Rémond and André Rîpoche built the « phasotron », a remarkable electronic equipment devised to average records of evoked potentials. According to Robert Naquet, the *phasotron* “was intended to give a topological representation of EEG records, as well as the usual temporal data. Gastaut received the first apparatus order, a truly *armoire à glace*¹²! Surprisingly, the phasotron had no breakdown and gave the same results in 1962 the PDP¹³ would give in later years: the results obtained were astonishing for such a remote period¹⁴. No commercialisation was ever planned. However, a second apparatus was made in Marseilles for the laboratory of Henri Gastaut, thanks to special funds from the US Air Force.

The industrial manufacture and marketing of electroencephalographic instruments by the French companies Alvar and ECEM never reached the level of expansion of the American Grass company involved in the race for patent deposit. Albert Melvin Grass (1910–1992) initially hired at the Physiological department at Harvard funded the renown Grass company with his wife¹⁵. No such transfers from the academic to industry occurred in France in the field of neurophysiology. However, French scientist had the knowledge for technological innovations and to make new instruments out of older ones¹⁶.

Together with the electroencephalograph maker Frank Offner, Rémond further devised the MATIDE system to extract spatiotemporal data from EEG records¹⁷, but without any marketing. Rémond never created any company, unlike Offner who created *Offner electronics*. The CNRS never accepted Rémond worked in a hospital with patients while devoting much of his time to technological innovation. He was finally obliged to focus on fundamental research only.

In general, French technological innovations in the field of neurology and neurophysiology remained local at the level of laboratories collaborating with small companies for their own needs, without large scale commercialisation. French scientists did not take part to the marketing of their instruments in this field in the twentieth century.

¹⁰ Pierre Buser acquired electronic skills during Second World War as a radio officer, which helped him to build his own differential amplifiers after war.

¹¹ David Whiteridge gave Fessard electronic parts after the war.

¹² A huge ice cabinet.

¹³ The first computer built by the American company Digital Equipment Corporation (DEC) in 1959.

¹⁴ B. Renault, R. Naquet. Antoine Rémond, 15 janvier 1917 – 5 juillet 1998, *Clinical Neurophysiology*, 29, 374-378

¹⁵ S.J. Zottoli. The Origin of the Grass Foundation, *Biol Bull*, 2001, 201, 218-226.

¹⁶ Two polygraphs were each taken apart and reassembled in the laboratory of Alphonse Baudouin.

¹⁷ MATIDE was an automated system, as those initially created by Grey Walter in the forties, as his *Low frequency analyser* (1943).

However, in the nineteenth century, science and industry were brought ever closer. Scientists were recruited in large European companies such as Krupp¹⁸ (Essen, Germany), Schneider¹⁹ (Le Creusot, France), Les frères Lumière (Lyons, France). In the twentieth century, sophisticated industrial instruments entered biological laboratories (electron microscopes, ultracentrifuge, imaging systems), including in the field of neuroscience²⁰. However, French scientists remained devoted to public departments and never penetrated private companies as they did in the United States and Great Britain. The level of technological expertise does not explain such differences, since it was generally high, in part due to military training before or during the Second World War. Furthermore, engineers in electronics were hired as technicians in neurophysiological laboratories, where they helped their colleagues and sometimes became leading full-time research fellows (Georges Weiss, Denise Albe-Fessard, Alain Berthoz).

A new technological field was opened during the Cold War period with spatial research. French neurophysiology took part in the study of the physiological adaptations in low gravity conditions (microgravity), in the perspective of inhabited space flights. The control of microgravity during parabolic flights of missiles containing trained animals (monkeys)²¹, and airplanes, allowed the neurophysiological study of sense organs, particularly involved in balance. The interaction between space industry, military projects and neurophysiological research allowed reciprocal benefits, without real common goals.

¹⁸ E.C. McCreary. Social Welfare and business: The Krupp welfare program, 1860-1914, *The Business History Review*, 1968, 42, 24-49.

¹⁹ S. Boutillier, L'industriel et le militaire, éléments de réflexion à partir du capital social. Le cas des Schneider, *Innovations, Cahiers d'économie de l'innovation*, 2005, 21, 167-196.

²⁰ René Couteaux and Jacques Taxi from the Faculté des Sciences de Paris are the first French scientists to use the electron microscope in the study of the nervous system.

²¹ Arlette Rougeul-Buser recalls one such experiment. « In the sixties, scientists still debated on the capacity of an animal to execute actions requiring attention, memory, cognitive tasks and motor actions in the absence of gravity. The *Centre d'Études et de Recherches de Médecine Aéronautique* (CERMA) developed a scientific project to answer such a question at the Space center at Hammaguir (Sahara) with the Vesta Rocket. The parabolic flight allowed, at its highest phase, a 8 minutes period with no gravity. Several preliminary flights were undertaken with rats and cats with no damage. During these flights, recordings of the bioelectrical activity of these animals, at the cortical level as well as in deeper brain structures, with EEG, were made with implanted electrodes and telemetry of collected data transmitted to the ground level. Such recordings showed the appearance of slow rhythmic waves (4-6 Hz) specific to the period with no gravity. Then followed the flight of a female monkey, Martine, in order to test the capacity to execute a cognitive task involving motor action. The monkey had been trained at the ground level to press down a central button in a group of five in order to get fruit juice in the mouth at each push. During the flight, a camera was recording the animal's behaviour, while another was focussed on the hand of the animal. Also superficial and deep EEG signals were continuously recorded. The monkey had its coat fixed on a chair. During ascension, the animal behaved normally, performed the task with normal EEG signals. But, on the contrary, during the no gravity phase, the monkey remained immobile and did not press any button. EEG signals showed large 4-6 Hz waves characteristic of a lack of attention. Martine had its eye-lid almost closed and its facial expression showed discomfort and confusion. During descent, the animal had normal facial expression back and normal EEG signals. The animal performed the trained behavior again. After landing, technicians found Martine gently pressing the central button to get fruitjuice. What happened during the no gravity period? Slow waves are observed when a subject has no focussed attention [...] Perhaps the animal was dizzy as this is now observed in human subjects [...] This experiment asked whether or not a man would behave in a similar way ». Adapted and translated from http://www.capcomespace.net/dossiers/espace_europeen/espace_francais/veronique_vesta.htm.

Space research started with the making of missiles derived from the German V2, by Soviet and American scientists. In the fifties, space animal experimentation began with the idea of controlling physiological activities during flight. In the sixties and seventies, such experiments were made on rats, rabbits and monkeys. Evoked cortical potentials were measured on animal with implanted electrodes²². The neurophysiologist, Pierre Buser, studied with the *médecin général* Grandpierre, a conditional feeding behaviour in a trained monkey. The flights, lasting fifteen minutes, were organised by the *Centre de recherches de médecine aéronautique de Paris* in South Algeria, Hammaguir, south-west to Colomb-Béchar²³. The Vesta type rocket had an ascensional phase up to 240 km, and a 6-8 minutes parabolic fall in microgravity condition, followed by a descent of the capsule with a parachute. During the ascent, the monkey behaved normally, as it was trained to, seeking food with a conditional paradigm. Under microgravity, the animal stopped its conditional behaviour, his eyes were half-shut, its brain showed slow waves in the EEG records, suggesting drowsiness or faintness. Buser concluded from this experience that "it taught us observations could be made, with limited means, which were not refuted [...] [to his knowledge] with modern investigations"²⁴.

These relations between space research and neurophysiology occurred during the Cold War, in the context of an international competition for animal space flights, when the dog Laïka sent in Spoutnik satellite became a Russian symbol. The French political position of Général de Gaulle promoted Franco-Russian space cooperation during the sixties. Numerous biological experimentations were made at Saliout station. Alain Berthoz, from the Collège de France, pursued such experiments in the following decades with neurophysiological studies of the vestibular system during Spacelab-1 mission²⁵. Franco-Russian space cooperation was first exclusively scientific before it turned out to industrial and commercial projects after 1996²⁶. From this point of view, scientific cooperation within missions related to space, army and industry could lead to future industrial and commercial innovations.

Common scientific and industrial projects in space research program of the fifties and sixties were not very productive. Nevertheless, key observations were provided to industry in a preliminary stage of investigation of new domains such as inhabited flights. Experimentations were set up by academic laboratories which provided high level and

²² G. Chatelier. Les premières expériences biologiques françaises en fusée, in *L'Essor des Recherches Spatiales en France: Première rencontre de l'I. F. H. E.*, Brigitte Schürmann, éd., European Space Agency, ESA SP-472, 2001, pp. 81-99.

²³ See note 22. See also Pierre Buser. Premiers vols français d'animaux en microgravité, in *La recherche spatiale française, Rapport sur la science et la technologie*, N°22, Académie des Sciences, 2006, EDP Sciences, Les Ulis, pp. 115-116.

²⁴ Ibid., p. 116.

²⁵ L'espace au service de la recherche scientifique. Académie nationale de l'air et de l'espace. Commission espace.

²⁶ Rapport de l'Assemblée nationale, n° 3438, enregistré à la Présidence de l'Assemblée nationale le 5 décembre 2001, fait au nom de la commission des affaires étrangères sur le projet de loi, adopté par le Sénat, autorisant l'approbation du protocole à l'accord entre le Gouvernement de la république Française et le Gouvernement de la Fédération de Russie relatif à la coopération dans le domaine de l'exploration et de l'utilisation de l'espace à des fins pacifiques en date du 26 novembre 1996, fait par René André, député.

diversified expertises, with the possibility of employing independent teams, either competing, or enabling the comparison of data. To this end, private industrial innovation always requires strong academic research. For public laboratories, these collaborations were a means to obtain funding and to establish long lasting relations with industry.

The field of ergonomy is another example where physiological sciences and industry were brought together within the discipline of the physiology of work. Lahy, Laugier, Piéron and Toulouse clearly saw an interest in the scientific study of work in industry for the selection of workers and the optimization of work²⁷. In January 1925, Lahy founds at the *Société des transports en commun de la région parisienne* (STCRP) the first French technical service in a private company with the aim to properly select wattmen to reduce accidents and the cost of professional training with a focuss on reducing electricity consumption and equipment wear. Lahy developed tests to measure fatigue, reaction times and perceptive discrimination, as well as emotions (psycho-galvanic reflex), motor suggestibility, movement anticipation, verbal memory and diffuse attention with sophisticated instruments with the help of engineer, Gaston Guyot (1879-1943), who later was the first director of the service²⁸.

The *Institut national d'orientation professionnelle* was founded in 1928. At the *Conservatoire National des Arts et Métiers*, a chair was created for Henri Laugier on these topics, in relation to industry. The young Alfred Fessard studied muscular synergies on Paris subway drivers with Laugier. Lahy set up psychotechnic methods for the selection of pilots which the French Army used during the Second World War. It can be concluded that, between 1945 and 1975, the physiology of work maintained close connection with neurophysiology benefiting from contacts with industry on ergonomic projects, and this tradition was kept alive with Alain Berthoz at the Collège de France in the following decades²⁹.

The relations between sciences and their applications in the making of neurophysiological instruments show a rather linear model, although bidirectional. This can be seen in the progressive making of mechanical and optic devices of Lucas and Adrian, in the development of the differential amplifier by Matthews and Toennies, or in the technological innovations of stereotaxy. However, in other domains, the triple helix model of science/industry/government relations, suggesting strong and local trading zones, seems more appropriate³⁰, in particular if we want to describe relations between neurophysiology and industry in space research and ergonomy. In fact, political and industrial administrators were aware of such converging spaces, well before their conceptualisation in the social sciences of

²⁷ W.H. Schneider. The scientific study of labor in Interwar France, *French historical studies*, 1991, 17, 410-446.

²⁸ Michel Huteau, D. Guyot & R. Simonnet. Un siècle de psychométrie et de psychologie. Établissements d'applications psychotechniques, *L'orientation scolaire et professionnelle*, 37/3, 2008, 441-444.

²⁹ When Alain Berthoz opened his new laboratory at the Collège de France, he did not have, properly speaking, any ergonomic project, but some on the physiology of work. Some of these projects could in principle be beneficial to the medicine of work. Contracts were signed with industries on specific projects, with ESSILOR, Renault on vision and space orientation. According to Berthoz, public research cannot solve the complex problems of interest to industry. Industrial cooperation helps funding the research programs of scientists, while their results help to better understand the big questions industry asks.

³⁰ H. Etzkowitz, L. Leydesdorff. The dynamics of innovation: from National Systems and "Mode 2" to a Triple Helix of university-industry-government relations, *Research Policy*, 2000, 29, 109-123.

research and technology³¹. The INSERM, the *Institut national de la santé et de la recherche médicale*, was created in such a perspective in 1964, to favour industrial innovation in medicine in hospitals together with universities and industry. Ten years later, the national decree of May 9th 1974 clarified the mission of INSERM in the valuation of research, a trend which is still further required today.

In the field of neuroscience, neuropharmacology is the leading domain based on the INSERM model, where applications are both numerous and important. In the forties and the fifties, the pharmacology of mental diseases was often a matter of local collaboration between close chemists and neurophysiologists, sometimes in the same family. The young Antoine Rémond, CNRS research fellow at the Salpêtrière hospital, was trained as an electroencephalographist in the laboratory of his uncle Alphonse Baudouin. He studied epileptic patients and learned to prescribe drugs he studied with his father trained as a chemist. Rémond recalled: “I immediately realised that if I would add a methyl radical at some location of hydantoins, a drug which worked fine, but with side effects, the substance would be less toxic. I studied how the methyl could be added. I asked my father and we did it together. We made some. I studied it on mice. Progressively, I discovered how to articulate research and therapeutics. I found a pharmacist who told me we could sell the new drug. He wrote something of a patent and we sold methyl-hydantoin. This worked out nicely! Unfortunately, it was not industrially made. In the laboratory of the factory of my father, we could hardly make more. We made a few kilograms and this worked out for some time, then new and much better drugs appeared on the market and we gave up.”³²

The career of Henri Laborit can be seen as a rare example in France of a close relation between science, industry and army, although the position of Laborit had some drawbacks³³. Laborit is known for his discovery in the fifties of the psychiatric use of chlorpromazine tested on neuroleptic patients with psychosis of Pierre Deniker at Sainte-Anne hospital. Laborit was a military physician, then working at the hospital in Bizerte (Tunisia) on the potentiation of anaesthesia with antihistaminic drugs³⁴. Chlorpromazine was provided by Rhône-Poulenc Company, where the drug was put aside in pharmacological testing. Laborit tried it and realised the drug could be used as a *lobotomie pharmacologique*.

This discovery occurred in a converging space Laborit created as a military surgeon in relation with industry, while following his own research program. Nevertheless, Laborit was not in an ideal position. He had to fund his research with patents, he aroused little recognition from the academic world, and he was confronted to a strong competition with pharmaceutical industry which made new patents with molecules close to those found by scientists and physicians³⁵.

³¹ C. Limoges et al. *The new production of knowledge: the dynamics of science and research in contemporary societies*, Sage Publications, 1994, London.

³² Interview of Antoine Rémond made by Bernard Renaut in 1995. Reproduction with permission.

³³ J.N. Missa. Naissance de la psychopharmacologie en Europe et aux Etats-Unis, in *L'Essor des neurosciences, France 1945-1975*, C. Debru, Jean-Gaël Barbara, C. Cherici, eds., Paris, Hermann, 2000.

³⁴ J.N. Missa, 2008, *op. cit.*

³⁵ H. Laborit. *L'homme imaginant: essai de biologie politique*, Bourgois, 1990, Paris.

This story is very different from that of the discovery of halopéridol (Haldol) by the Belgium Paul Janssen in collaboration with the company of his father importing pharmaceutical drugs from Hungary³⁶. In the latter case, the family circle, reminiscent of the story of Rémond, was used to commercialise the drug. For Laborit, the trading zone he elaborated was not seen in France as a successful collaborating project.

The intensification of synergies, yielding new drugs, between neuropharmacology and industry benefited from the molecularisation of neuroscience. This process helped forging new and fruitful trading zones with the rise of biotechnology and the possibilities of discovery novel neurotransmitters, neuromodulators, their receptors, agonists and antagonists. As in other biotechnological areas, relations between science and applications are occurring in local companies created by scientists to develop their discoveries. This is most prominent in the eighties in France with the companies Bioprojet (1981), Bioprojet Pharma (1992, Tiorphan®), Bioprojet Biotech (2001), Pharmaleads (2008) who benefited from the work of Jean-Charles Schwartz and Bernard Roques in the seventies. Such science-industry spaces were under the control of scientists. However, collaboration with large pharmaceutical industries remained a source of funding for academic laboratories. Very few scientists from public laboratories moved to large pharmaceutical companies as this occurred more often in Great-Britain and the US³⁷.

In general, French public research was isolated from industry and its policy of patent deposit was slow and often non productive. This occurred in neuroscience as in other fields. The discovery of giant magnetoresistance by Peter Grünberg (Germany) and Albert Fert (France), 2007 Nobel Prize, highlights this general trend. Although Fert discovered the phenomena before his German colleague, it was Grünberg who obtained the patent which was highly profitable³⁸. However, Fert was regularly funded by a Thales (Thomson-CSF).

Neuropharmacology is a rare example where French scientists organise the ways their discoveries will be patented and marketed. This is rather new compared to many other fields of neuroscience. This trend was made possible by a clever management of patent deposits and by the changes in the nature of patents. Now, patents apply not only to chemically modified molecules, but also to genetically modified proteins as those developed by Alain Prochiantz in France³⁹. But the patenting of non material entities is not without problems. From this point of

³⁶ J.N. Missa, 2008, *op. cit.*

³⁷ L. Bonetta. On the move from Academia to industry: established neuroscientists who have made the transition from Academia to Industry are finding different rewards in a new environment, *J Neurosci*, 2007, 27, ii-iv.

³⁸ 10 millions euros were earned with the Grünberg patent. "This is significant of French research, a scientist reports. We have very brilliant scholars, but we do not manage to develop our work". *Le Figaro*, 22 octobre 2007.

³⁹ « Nouveaux facteurs de croissance neurotropes comprenant un peptide homéoboîte », Alain Prochiantz, A. Joliot Priority June 1990 N° 9006912. Extensions to European countries, Switzerland, Japan, USA and South Korea « Peptides utilisables pour l'adressage intracellulaire de molécules actives », Alain Prochiantz, G. Chassaing Priority October 1995 N° 95 11714. Extensions to European countries, Switzerland, Japan, USA and South Korea « Method for the identification of target genes of transcription factors », W. Wurst and A. Prochiantz Priority September 1997 N° 197 40 578.9-41. PLA 97A5. Extensions to European countries, Switzerland, Japan, USA and South Korea « Nouvelles applications de peptides issus du domaine cytoplasmique du précurseur de la protéine amyloïde », B. Allinquant, Alain Prochiantz. Priority July 1999 N° 99 09929 «

view, neuroscience is not in a favourable situation, since its objects of study are often complex and non material. They can be models and novel types of explanation⁴⁰. This may not be of a problem because the difficulties in patenting discoveries often enhance scientific exchange⁴¹.

The discovery of non material objects, but also of natural objects and natural phenomena are difficult or impossible to patent. However, scientists can describe patentable technologies making use of them in precise therapeutical procedures. A complex balance must then be found between patentable and non patentable objects for institutions to benefit from their discoveries⁴².

New biological domains will progressively strengthen neuroscience/industry connexions in the future. In particular automation will develop and novel automated systems will be devised to collect large amounts of data (genetic or electrophysiological) to create neuroscientific models in the spirit of systems biology. Also, man/machine interfaces and the industry of robotics will probably be developed⁴³. In the era of cybernetics, such approaches relied on self-made machines by extravagant and brilliant scientists. In particular, William Grey Walter was famous for leaving his automated turtles move around his wife and children. Neuroscience was then not integrated to industry in a general manner, as it now becomes.

Nowadays, a new field of neuroscience applications is bound to play a new role in courts of justice, when experts are asked to provide imaging evidence of lesions and tumours or functional evidence of the memory of past events. However, such procedures should rely on excellent and up to date scientific knowledge to act upon jury in unquestionable manners.

We conclude that neuroscience/industry relations were not highly profitable to French neuroscience or society between 1945 and 1975, due to intrinsic characteristics of this scientific field, as they occur in other countries, but also because of French difficulties in integrating public science to private companies and industry. Also, little was done to provide scientists a better knowledge of the procedures of patent deposit. However, the space opened by these relations was highly profitable to neuroscience and industry, although collaborative projects were rare. Many occasions were missed in the marketing of prototypes. However, connexions with industry became central for the funding of most laboratories, because of the progressive lack of public money. Some industrial projects were successful, most of them in the discipline of neuropharmacology.

Vecteurs de transport à travers un épithélium à jonctions serrées », E. Dupont, A. Joliot, Alain Prochiantz. November 20th, 2000, N° 0014945 « Expression cellulaire et tissulaire de gènes introduits par des phages cargos », E. Dupont, A. Joliot, A. Trembleau, M. Volovitch, Alain Prochiantz. January 2003.

⁴⁰ S.R. Kirschenbaum. Patenting basic research: myths and realities. *Nature neurosci supp*, 2002, 5, 1025-1027.

⁴¹ Ibid.

⁴² E.R. Ergenzinger, M.L. Cunningham, P.M. Webber, W.M. Spruill. Patenting neuroscience: challenges and opportunities in an interdisciplinary field, *Nature Reviews Neuroscience*, 2004, 5, 657-661.

⁴³ J. Butcher. On reflection: The industrialisation of neuroscience, *The Lancet Neurology*, 7, 386.

The new spaces opened between neuroscience and industry will provide models to future industrial developments of novel technologies such as man/machine interface, psychiatric surveillance and robotics, where neuroscience is expected to play a significant role in XXIth century. But most of all, industry is still expected to fund public research and to benefit from it in the acquisition of new knowledge elaborated by independent research programs from academic laboratories.