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Ethics and Neurosciences

Rapporteur: Mr Jean-Didier Vincent[1]

1 Director of the Alfred-Fessard Institute.

The brain manages all the relationships between the human being and the world around him; it is the organic core of the person, the agent of his freedom but also of the individual and social constraints which restrict that freedom. It endows man with culture and language. UNESCO is therefore the international organization to which it logically belongs. Significantly enough, our millennium is ending with a "Decade of the Brain" decided by the United States of America and later by the European Union. This importance is reflected in what are known by convention as the **neurosciences**, a new discipline which comprises both the biology of the nervous system and the sciences of man and society, together with the "hard" sciences (mathematics, physics), ranging from the most theoretical and abstract aspects to medical, technological and industrial approaches. Indeed, there are few areas of knowledge that do not touch upon the neurosciences. Through their creative power, these sciences hold out the hope of contributing to the greater well-being of man by relieving his pain, repairing his infirmities, improving his performance, prolonging his life and retarding the process of ageing. But they also pose a formidable threat by providing means of coercion and new sources of dependence.

This presentation does not claim to set out an exhaustive examination, however superficial, of the content of the neurosciences. Starting out from a few examples, we intend rather to put some ideas forward to the International Bioethics Committee of UNESCO (IBC). However, one can hardly broach the subject of ethics without first defining what is meant by the neurosciences and without looking at the historical background of their development.

I. Definitions

The "sciences of the nervous system" - a term which must not be confused with the neurosciences - did not see the light of day until the late 19th century with the combined development of physiology, histo-anatomy and anatomical clinical science. At the technical level, especially in the field of medicine, their spin-off remained relatively limited for a long time, but their ideological impact was considerable in the Western world: the *reflex theory* which associates every action with a stimulus, the *neuronal theory* which takes the view that the nervous system consists of an articulation of discrete elements or neurones, and *the theory of locations* which links the mental functions and faculties with specific areas of the brain, all influenced the materialist philosophies which served as a foundation for the great political movements of our century.

Paradoxically enough, psychology, which was long considered inseparable from philosophy, did not become an experimental science until it chose to ignore the brain and concentrate on behaviour regarded as a pattern of learning and the product of associations between stimuli and responses, inputs and outputs, without reference to the intermediate nerve mechanisms contained in the "black box". Later, the growth of ethology based on rigorous observation of animal behaviour caused attention to turn once again to the nerve structures underlying stereotyped and innate forms of behaviour. A first synthesis was made in the late 1950s between experimental psychology, ethology and physiology, largely as an outcome of the development of techniques to study the brain directly by fitting intracerebral electrodes to record the electrical activity of the structures or to stimulate them. In the field of medicine, this was the era of neurosurgery and psychosurgery.

The 1960s brought a veritable revolution with the discovery of the chemical messengers used by the nerve cells to communicate between themselves and the identification of their receptors. This upsurge of pharmacology and biological chemistry led to the development of medicinal preparations which actively influenced certain forms of behaviour or mental states and were capable of sedation or of alleviating symptoms. In medicine, this period corresponded to a renewal of psychiatry which took pathogenic concepts on board and acquired a highly effective arsenal of therapeutic instruments.

Computer science provides a theoretical model for understanding the brain; the analogy with the computer serves as a frame of reference for what are known today as the cognitive sciences. We are now witnessing, firstly, the creation of intelligent machines (artificial intelligence) and, secondly, the study of the processing of information involved in the brain functions in animals and man. The techniques of cerebral imaging, made possible by computer science, permit an increasingly precise visual display of the activities of the different regions of the brain and provide an anatomical foundation for the study of complex functions which cannot be shown by formal logic and derived algorithms alone.

Genetics and molecular biology have been the fundamental advancements of the last ten years. It is generally accepted that the genetic patrimony of a human being comprises some 100,000 genes; the brain structure alone uses more than 50,000 of them. Although their functions are not always known, new genes expressed in the nervous system are constantly being discovered. We shall see later the hopes and fears that this harvest of new knowledge is creating in the area of gene therapy which was the subject of an earlier report for the IBC in 1994.

A final, and in our view essential, phase involves the study of the development of the brain during the evolutionary processes (phylogenesis) and in the individual (ontogenesis). The discovery of regulating genes, guiding and adhesion molecules, cell growth and death factors enables us, by explaining the structure of the brain, to understand how it works and opens up demiurgic prospects for its subsequent transformation.

All these disciplines, which have undergone successive phases of development, constitute the field of the neurosciences today. After a brief outline of the neurosciences, noting their successes and failures alike, we shall turn to their technical and instrumental impacts, in particular their therapeutic spin-off and increasing social impact. We shall endeavour to view all these processes from the ethical standpoint.

II. The State of the Neurosciences Today

We shall look successively at the fields in which we believe the most significant breakthroughs have been made, and those in which progress has been less spectacular, to say nothing of disappointments and failures.

II.1 Breakthroughs

1. The techniques of cerebral imaging enable the brain to be observed at work and the level of activity of clearly defined regions to be known during the performance of various mental tasks. With three-dimensional reconstitution and rapid scanning nuclear magnetic resonance, man is now able to watch his own brain thinking.

2. At the level of the cells, we are perfectly familiar today with the nature of the nerve influx and the various electrical phenomena which confer upon the neuron its properties of excitability and its information-processing capabilities. Biophysical or "patch-clamp" methods provide direct access to the ionic channels and enable us to understand the way in which chemical messengers and their receptors act.

3. At the molecular level, in addition to identifying the structure of the channels, neurotransmitters and their receivers, the identification of an abundance of molecules which interact in cascades enables us to understand the functional and molecular substrates of fundamental phenomena such as pleasure, suffering, dependence, memory and the formation of cognitive maps in the brain. A new and promising field is that of development, with the discovery and isolation of growth factors, adhesion molecules which ensure both the genesis and cohesion of structures and, more recently, the molecules which are involved in guiding the nerve fibres whose connectivity reflects the complexity of the organization of paths and networks in the brain.

4. Genetics have been particularly fertile in the area of the neurosciences, revealing families of genes for the enzymes, receptors and linking proteins which take care of the different neuronal functions. The discovery of regulating genes, which are responsible for the development of the brain according to the plans of the species exposed to the influences of its environment, holds out considerable prospects not only for the understanding of the phylogenesis of the brain but also of the way in which it works. In the field of pathology, identification of the gene and of the nature of mutation has been possible in some monogenic pathological conditions of the nerve system, the most spectacular example being Huntington's chorea.

II.2 Less Successful Advances and Disappointments

In drawing up a scientific balance sheet, it is not usual practice to call attention to failures. The media take an interest in spectacular successes. They sometimes fail to report the disappointing outcome of the results announced in a blaze of publicity, preferring instead the spontaneous concert of voices which transforms research into a triumphal avenue.

II.2.1 Medicinal Preparations

Despite the considerable efforts made by institutional research and by the pharmaceutical industry, no genuinely new family of molecules has appeared in the last decade. It is true that a better understanding of the potential targets in the brain, in particular as a result of genetic identification of the receptors for neurotransmitters, has enabled the number of active molecules to be multiplied and their indications better adjusted to patients' needs. But these sporadic discoveries cannot be compared with the revolution represented by the appearance several decades ago of the first tranquillizing and antidepressant molecules. Moreover, there is good reason to wonder whether the world-wide success of some products on the market for psychotropic substances does not reflect an effective marketing campaign rather than real therapeutic originality.

II.2.2 Computer Science

Artificial intelligence is a particularly fertile branch of computer research, notably in the area of robotics and expert machines; on the other hand, its contribution to the understanding of the cognitive functions of the brain has proved disappointing. The significant advances brought about by computer science remain confined to the technical sphere - for example, imaging or the processing of electrophysiological data.

II.2.3 Intervention in the Brain Itself

After the use of neurosurgery as a palliative measure to treat neuro-degenerative conditions of the brain such as Parkinson's disease or serious behavioural problems, a genuinely substitutive therapy was proposed in the shape of the transplantation of embryonal nerve cells within degenerative or damaged cerebral structures. The complexity of the problems raised and the absence of any long-term follow-up suggest a need for extreme circumspection here.

II.2.4 The Genetics of Hereditary Diseases

The genetics of hereditary diseases is complicated by the rare nature of monogenetic conditions, our highly inadequate understanding of pathological mechanisms and the total lack of therapeutic solutions in the near future. The most convincing results are of a diagnostic nature and openly raise the problem of eugenics. Here again it is to be feared that the publicity given to a few spectacular results may create unfounded hopes among patients.

III. The Impact of Neurosciences

This occurs firstly at the instrumental level, which comprises medical and technical aspects, and secondly at the level of society.

III.1 The Instrumental Impact

This touches upon the diversity of the techniques and disciplines involved in the neurosciences.

III.1.1 New Molecules

The techniques of molecular biology and genetic engineering enable substances whose cell functions are often unknown to be obtained. We are in the presence of a Pandora's box which, when it is opened, may well release potentially dangerous substances. Cloning of the receptor of *tetrahydrocannabinol*, the active principle of cannabis, was rapidly followed by the discovery of its endogenous ligand, *anandamide*, whose original chemical structure and mode of secretion by the nerve cells might lead on to the development of a new family of medicinal substances, the danger being that these may also extend the list of addictive substances. That is the reverse side of the coin encountered whenever psychoactive substances are launched on the market. The anxiolytics, and in particular the benzodiazepines whose receptors in the brain have now been identified, have a relaxing and anticonvulsant sedative effect. This effect is beneficial when the substances are administered for therapeutic purposes but heavy dependence also occurs; these substances can therefore be classified as drugs alongside illicit substances.

All molecules with a psychotropic action must of course undergo therapeutic testing on human subjects. These tests pose specific problems associated with the mental state of the patient. He may be in a state (agitation, violence, intolerable moral suffering, suicidal tendency) such that it would be totally incompatible with medical ethics not to prescribe a substance which has an effective action. In contrast to that basic principle of prescription, it is desirable - in order to prove that a new molecule has a specific psychotropic effect on depressed patients - to conduct tests against placebos and not, as is normally done, against a reference product. This kind of therapeutic test can be performed only on condition that the following recommendations are followed:

a) the study must on no account include adult patients who have refused or were unable to give <u>genuinely enlightened consent</u> or those whose <u>condition and case history are so serious</u> as to necessitate immediate use of a proven form of therapy;

b) patients in hospitals must be placed under close medical surveillance in specialized units which are trained in the <u>prevention</u> of suicidal behaviour;

c) the experimental protocol, which will be brief, must provide for the possible <u>premature discontinuation</u> of the test and replacement of the tested treatment by a reference product;

d) a long-term evaluation of the risks incurred will relate, in particular, to the dangers of dependence and tolerance;

e) therapeutic testing on children poses particular problems. The medical treatment contract is based on the consent of the patient; in the case of children or adolescents, it is vital to obtain the agreement of their parents or guardians. When children are involved, the problem of obtaining the consent of the child himself arises when he reaches the age at which he may be regarded as capable of understanding the principle of the treatment and possibly of declining it. Children are thought to be consciously capable of this decision from the age of 9 or 10 and they should therefore be given information in a manner which accords with their level of cognitive and emotional development. However, in psychiatry, many children may show, to varying degrees, retarded or distorted faculties of judgement and understanding. In consequence, it is more logical to refer to their mental age rather than to their chronological age.

   The situation in regard to consent obtained from legal representatives is not always easy. For example, there may be a disagreement between the two parents or between the parents and the child (divorced couples, children who have been the victim of abuse, etc.).

   For the consent to have real value it must be freely given and enlightened; compliance with those conditions by the parents is not always easy to secure. Obtaining consent from the parents may not be sufficient in some cases to protect the rights of their handicapped children. The mere fact of having a child with a severe handicap may lead the parents and professional specialists to modify, albeit in a subtle and involuntary manner, their ethical standards in relation to these children. There are examples of research performed on mentally handicapped children with the consent of their parents under unethical conditions. The administration of psychotropic substances to children is extremely widespread in some countries and is sometimes based on insufficiently verified psycho-pathological assumptions, e.g. the administration of amphetamines to hyperkinetic children.

One last risk must, in our view, be highlighted in respect of the therapeutic indications of new molecules, i.e. the abusive widening of the field of prescription. Some pharmaceutical substances with a specific action on serious psychotic states may be administered to a patient during minor mood or affectivity episodes that do not in themselves justify the use of molecules which have secondary effects and are not without long-term risks. For example, it may be dangerous to extend the prescription of palliative remedies that are useful in neuro-degenerative conditions of the brain to purely preventive indications, e.g. against ageing. With profits in mind, pharmaceutical companies and prescribing doctors may sometimes be tempted to give in to strong social pressure.

III.1.2 Neuro-technology

The rapid pace of development of computer science enables us to suspect the future importance of an area of the neurosciences which has as yet hardly been explored, i.e. the creation of chimeras no longer associating animal tissues of different origins but bringing cerebral tissue together with what might be termed an electronic tissue. In the present state of knowledge, we have prostheses which are capable of replacing and repairing a damaged sensory or motor system. In future, the implantation in the brain itself of microelectronic circuits might be envisaged to replace or supplement higher cognitive functions. The ethical problems posed by such techniques are not so very far removed from those raised by implants of animal tissue, e.g. foetal nerve cells or strains selected or converted with a view to the secretion of specific chemical agents.

The field in which the use of microelectronic implants has made the most progress is that of cochlear implants and, to a lesser degree, retinal implants. The technique of the cochlear implant consists in introducing a number of stimulating electrodes into the cochlea; these electrodes activate the fibres of the acoustic nerves by means of electrical pulses whose characteristics are determined by those of the sound signals received by the subject. The ethical problems posed by the use of a prosthesis of this kind are far more complex in the case of young children suffering from severe deafness before learning to speak, i.e. "prelingual" children, than in persons who have become deaf after learning to speak. Firstly, these "postlingual severely deaf subjects" who are generally adults can themselves take the decision to have an implant. Secondly, it is possible to make a sufficiently objective assessment of the effectiveness of such a prosthesis. Overall, the results are positive. The epigenetic traces left in the central nerve structures involved in the learning and prolonged exercise of oral communication probably play a favourable role in the restoration of satisfactory oral communication.

The situation is quite different in the case of prelingual deaf children - firstly, because the decision to make the implant is taken by parents who are often disturbed by the deafness of their child and, secondly, because insufficient objective data is available to assess the effectiveness of the implants. In addition, we do not yet know how the central nerve structures which have received very little acoustic information will treat the information supplied by the prosthesis, which differs substantially from the physiological information.

In its Opinion n°44 of 1 December 1994, the National Ethical Consultative Committee for the Sciences of Life and Health of France (CCNE) expressed the view that as long as uncertainty prevailed, everything must be done to avoid jeopardizing the cognitive development of these children. It recommended the association of cochlear implants with tuition in the use of sign language whose effectiveness in this area is proven. With this sign language, children will have a mode of communication that will enable them to ensure their cognitive development and psycho-affective equilibrium. On the other hand, systematic limitation to the learning of sign language was not felt desirable by the Committee as it would deprive the children of the possibility of learning the oral language. In short, the CCNE favours bilingual education in prelingual deaf children.

At a world conference on the brain-computer interface, the German Academy for the Third Millennium proposed a charter governing neuro-technological research. On the whole, this charter suggests the same rules of caution and long-term follow-up as have been applied in the case of other manipulations of the brain.

III.1.3 Genetic Manipulations

The discovery of the brain development genes, and the role that some highly discrete genetic modifications may have played in the cerebral development of pre-human primates, leads us to envisage frightening possibilities of interference with the development of the human brain. The absolute rules protecting the germline do, for the time being, shelter man from any such misguided, "demiurgic" temptations.

III.1.4 Intervention to Enhance Human Performance

For the most part, these are techniques which permit intervention to influence human behaviour and the cognitive abilities of individuals and groups. The objectives are to understand the skills and performance of the human being during the different periods of his life, in both habitual and exceptional situations. These methods range from straightforward observation in the natural or standardized situation to tests of reactions under "extreme conditions". Subjects are recruited on a voluntary basis. The sub-disciplines that have been identified are: psychology of the child and development, social psychology, cognitive psychology, psychology of work, ergonomics, psycho-linguistics, psychopathology, clinical psychology, neuropsychology, psycho-pharmacology. There are many interfaces with neighbouring disciplines: anthropology, neurosciences, psychiatry, linguistics, sociology, educational sciences, artificial intelligence, etc. The main lines of the directives on research involving human beings formulated in the United States of America by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1974-1978) or in Canada by the Medical Research Council (1986) and later by the National Council on Bioethics in Human Research (NCBHR) are identical to those applicable to all research on human subjects in the biomedical and human sciences. More recently, they were embodied in the Opinion of the CCNE (n°38, October 1993) on research in the behavioural sciences.

We shall confine ourselves here to drawing attention to a few specific aspects:

a) Under what conditions is it permissible to perform behavioural research on subjects whose ability to consent is doubtful (limited competence, dependence)? The vulnerable categories requiring special protection in behavioural research are: children, the mentally handicapped, persons who can easily be manipulated because of a specific weakness or dependence (e.g. drug addicts), captive institutionalized populations (prisoners, pupils, adolescents in supervised education, young people in homes, members of the armed forces, refugees).

b) How can the obligation to secure enlightened consent be reconciled with the methodological need (which may be encountered in some experimented protocols) of not telling the subject everything? In other words, what frontier can be drawn between deliberate deception for research purposes and manipulation of the individual?

c) Another major ethical problem is posed by the sharing, for research purposes, of medical and/or psychological information about individuals; this is currently prohibited in France by law and by the code of medical ethics. The CCNE for its part takes the view that some research of acknowledged interest may be performed in a context of shared professional secrecy. If, for the purposes of their research, psychologists need to process under their own responsibility certain medical data identified by the name of the test subjects, these psychologists would have to be given "special authorization" and the medical practitioner must have been explicitly authorized by the persons concerned to divulge this data. The same requirement applies, by corollary, to practising psychologists.

It would seem desirable for research protocols in the sciences of human behaviour to be presented, before the research is performed, for an opinion to committees which might be "consultative committees for the protection of individuals specializing in behavioural research"; their membership would have to guarantee a sufficiently wide representation of professional expertise.

Their purpose would, in particular, be to guarantee that the freedom and security of subjects are protected:

- by making sure that the proposed experiments do not pose a threat to the security or dignity of the participating persons;
- by assessing the procedures laid down for informing and obtaining the consent of the persons taking part in the study, especially when that information has to remain incomplete in the initial phase.

These investigations should also evaluate the psychological and behavioural therapeutic methods which are all too often left to the sole discretion of the researchers concerned.

III.2 Social Impact

1. Here we shall draw attention first of all to the delicate relationship between the neurosciences and the media or, more generally, public opinion.

2. Nowadays, the science of genetics wields considerable power over the human imagination. There is a strong temptation to associate the different forms of deviant behaviour and, more generally, all the character traits of an individual with genetic determinism. We can observe the publication and disclosure to the general public, often without the necessary precautions, of references to the gene of homosexuality, aggressiveness or even the gene of crime, etc.

3. When it comes to deviant forms of conduct, notably in sexual matters, there is a choice between preventive detention or the use of chemical substances which act directly on certain nerve centres and by doing so diminish the libido without, however, totally precluding the possibility of a repetition of the offence. Tolerance and respect for the autonomy of the individual must be weighed up against the social threats that an individual may pose.

4. Finally, the neurosciences lie at the heart of the immense problem of drug dependence which will not be dealt with in this report.

IV. Conclusion

This Report has no ambition other than to show the extensive scope of what are referred to today as the neurosciences. We must of course point out that Man, in his natural and cultural dimensions, is always present on the horizon of each of the many constituent disciplines involved. While the neurosciences do bring hope, notably in the area of mental health, they are also a particularly dangerous terrain for genetic manipulation and for the use of pharmacology and computer science for behavioural ends. As a possible instrument of encroachment on human liberty and dignity, the neurosciences may also turn out to be a poisoned chalice on which the worst forms of ideology may thrive. The purpose of this report is to examine in a clear-sighted way and without complacency, the hopes and risks involved and to issue a few warnings of an ethical nature.