Brain Chemistry and Mental Functions

Ricardo Tapia.

The effects of so-called psychotropic drugs, including all those that affect mental activity, have concerned, impassioned and worried humans for millenia. How could one not be interested in substances that, as they are ingested, inhaled or injected, produce alterations of consciousness, perception, even personality? However, it wasn't until the discovery – only about thirty years ago – that the communicating mechanism between neurons inside the brain is biochemical in nature, that an idea started to form –to date still imprecise and hypothetical – on how these drugs might act.

The reasoning is simple: if the neuron circuits and networks that constitute the brain (formed by about 100 billion neurons topographically organized in a specific manner), require a chemical mechanism in order to function, and if psychotropic drugs are, by definition, chemical substances, it seems possible that they act by interfering or modifying communication patterns between neurons. Thus, we can make a far-reaching conclusion. If what has been previously said is true, the mind therefore must function through neurochemical mechanisms.

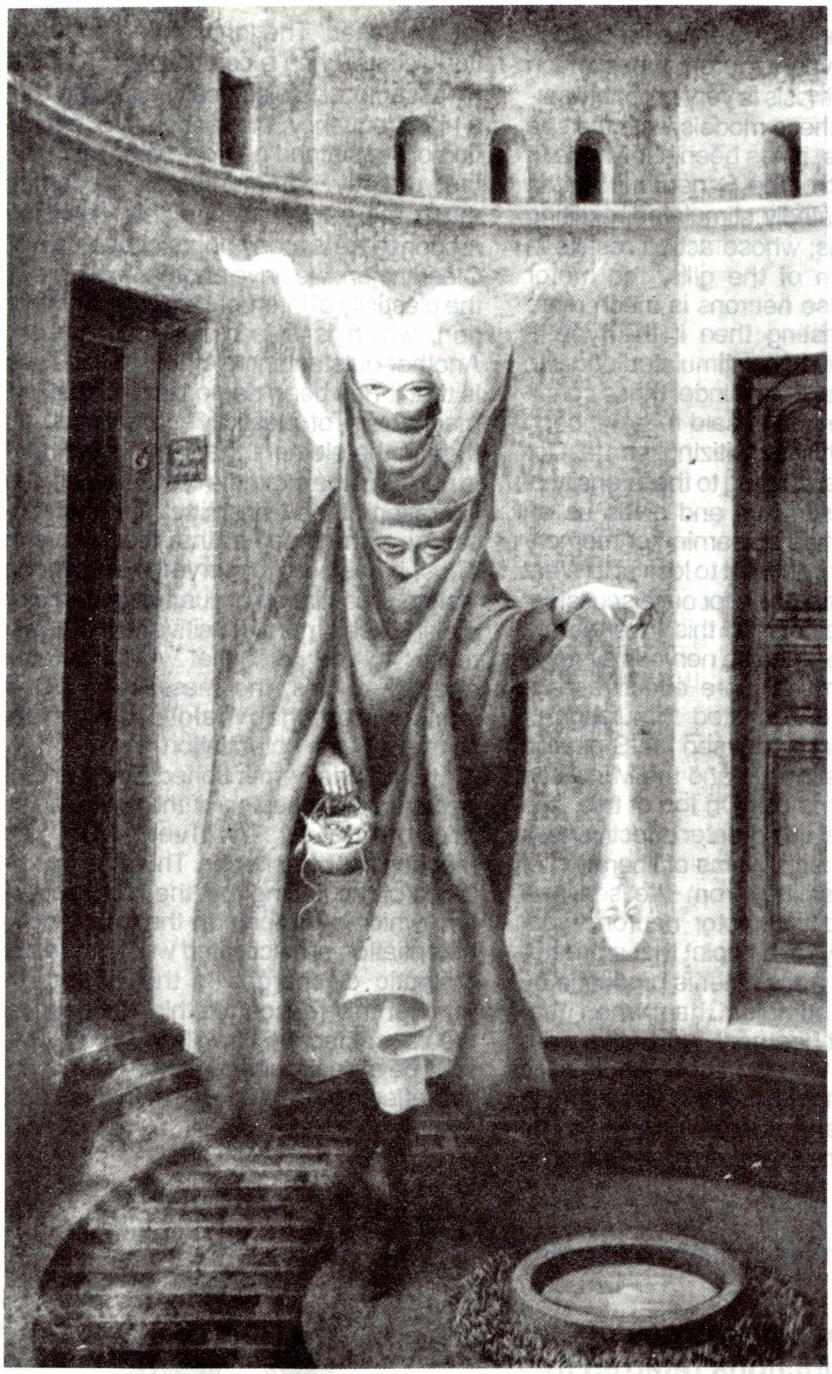
Clearly, the intentionally provocative previous paragraph synthesizes in a few lines what could be a sizeable book, full of facts and arguments. But for the purposes of this essay, it is useful because it underlines our aim, which is to set forth the importance of bio-chemistry in brain functions, through a short exposition of the following aspects: a) the chemical mechanisms that allow neurons to communicate with each other; b) some experimental data that suggest how such mechanisms can participate in memory and learning processes; c) the neurochemical way certain commonly used drugs act; and d) a speculation, based on the above points, about how brain biochemistry might be the basis for mental functions.

Researcher, Institute of Cellular Physiology, UNAM.

Chemical Communication Between Neurons

The chemical language used by neurons to communicate esentially includes three elements: the emission of a message by a neuron, its reception by a second neuron and its transduction to a different state of excitation of the second neuron. The message is eminently chemical in nature, since it is a specific substance that the neuron synthesizes inside and releases towards the neuron it communicates with. This one, in turn, is able to receive the information through large molecules located on its membrane, and which have a region that projects towards the cell's exterior.

This part, which faces the emitting neuron, recognizes the messenger sent and accepts its joining it, due to the affinity or complementarity that exists between the chemical structures of the messenger and the acceptor. As a consequence of



Woman leaving the psychoanalyst, by Remedios Varo. Reproduction by Alejandra Novoa

A long lasting potentiation occurs when a certain neuron of the hippocampus is electrically stimulated at a high frequency

this union, certain physical-chemical changes occur in other regions of the acceptor molecule and/or other large molecules that are embedded in the membrane and associated to the acceptor molecule. Finally, these changes determine the message's translation or transduction into a state of greater (or lesser, according to the type of interaction between the messenger and its acceptor), excitation of the whole neuron, which can last, from fractions of a second, to two or three minutes, depending on the type of transduction that takes place. Thus, the three elements of interneuron communication are, a neurotransmitter neuron (the messenger), a receiver one (in the membrane) and a transduction mechanism.

This biochemical mechanism demonstrates that interneuron communications have several interesting and important properties: 1) Communication is essentially unidirectional: one neuron emits a message and the other receives it, but not the other way. 2) As a result of the message's type of transduction (which depends on the chemical nature of the neurotransmitter and the receiver), the neuron can become excited or inhibited, that is, active or inactive, for short or comparatively longer periods. 3) Since the neuron has the capacity of neurotransmitting and receiving molecules, communication between neurons can become more or less efficient, that is, it is a malleable and a plastic communication. This last property is the one most obviously related to this essay's subject, given its consequences as regards one of the most evident and amazing properties of the nervous system: to modify itself as a result of previous experiences.

Plasticity in Communication Between Neurons and Learning

Let's consider a very simple hypothetical learning model: one neuron which we will call the motor or M upon whose action depends a specific conduct, for example, a quick movement of flight. We have another neuron (the sensitive one or S), that upon perceiving a certain signal from the environment excites the M neuron to generate this reaction of flight. Let's ask the following question of this system: given the plastic capacity of the communication between these two neurons, is it possible that its efficiency increase as a consequence of repetition of the signal from the environment, in such a way that the final response of escape happens more quickly? If the answer to this question is affirmative, we can conclude that the system has learned to respond better to the stimulus when this occurs more frequently.

There are various experimental biological models of very different types which show this hypothesis is very probably correct. In one of these models, with the sea mollusk Aplysis, it has been shown that if a structure with type S neurons of the animal is repeatedly stimulated, exciting type M neurons, whose action results in the contraction of the gills, the motor reponse of these neurons is much more intense and lasting then if the type S neuron had only been stimulated once. In neuro-biological terms under these conditions the M neuron is said to have been "sensitized". This "sensitizing" can last for hours or days according to the intensity of the repetitive stimulus and gives us an excellent example of learning or memory whichever way you want to look at it. What is most interesting here for our discussion, is that this memory (in this invertebrate which has a very simple nervous system) has become much more effective as a consequence of repeated stimulation of the communicatin between the S neuron that feels the stimulus and the M neuron which moves the gill. On top of this, it is also known that this greater effectiveness is due to the mechanisms of liberation of the neurotransmitter from the sensitive neuron toward the motor neuron, work more efficiently to the point that a greater quantity of the transmitter is produced by the received stimulus than when that animal has not "learned". And if this were not sufficient, we also know the specific cause of the increase of this liberation, in terms of changes that occur in the molecules of the S neuron participating in this liberation.

We cannot imagine any of the mental functions referred to before -for example, the conscience- if the mechanism of memory did not exist

Another very interesting example of the increase in the efficiency of interneuronal communication as a consequence of repeated stimulation is the phenomenon known as "long lasting potentiation". This has been described in a brain structure of mammals known with the suggestive name of hippocampus. This structure carries out numerous important functions and is involved, among other things, in the production of epilepsy when its neurons are damaged. The long lasting potentiation occurs when a certain neuron of the hippocampus is electrically stimulated at a high frequency, the response of excitation of the second neuron, with which the first directly communicates, becomes much more intense, and this amplified response lasts many hours or even days. Clearly then, we have another example of the plasticity of interneuronal communication, which is a learning phenomenon. Another outstanding element in this case is that it has been demonstrated that the mechanism of plasticity is chemical, although the element that is modified here is not, as in the example of the Aplysis, the liberation of the transmitter, but the sensitivity of the receptor that recognizes it. Thus, it has been observed that the long lasting potentiation is due to the receptor making itself more sensitive to the transmitter, to the point that with the same quantity of this, the message is better transducted than before the establishment of the potentiation.

It was briefly mentioned that the hippocampus is a region of the brain that is predominately involved with the mechanism of epilepsy. Thus the importance of the finding that the same receptors which participate in the long lasting potentiation are activated when there are epileptic discharges in the hippocampus.For this reason we think that one of the causal factors of epilepsy could possibly be a plastic phenomenon, with negative effects for the organism in this case,

Engraving by Arthur Boyd, 1870. Reproduction by Alejandra Novoa

Neurons in most regions of the brain release a transmitter, which interacts with its corresponding receptor and inhibits the excitability of these neurons

but similar in its molecular mechanism as being responsible for facilitating interneuronal communication.

The experimental examples we just described show without a doubt the participation of the brain's chemistry in the phenomena of plasticity of interneuronal communication. From this we can also see its importance in the mechanisms of learning and memory. These processes have an undoubted relation with mental activity, since we cannot imagine any of the mental functions referred to before –for example, the conscience– if the mechanism of memory did not exist. However, it is clear that there is a difference between this and mental activity. What we have said up to now does not allow us to state that there is a direct relation between brain chemistry and the mind. However, there are other facts that allow us to look more closely at this problem.

Etching by Francisco Goya. Reproduction by Alejandra Novoa

Modifying Interneuronal Communication

One of the drugs most used today to diminish anxiety is valium. Millions of individuals all over the world take it almost constantly to feel more at ease and healthy with the continuous stress of city life at the end of this twentieth century. This drug belongs to the group of the benzodiacepinas, whose mechanism of action on the brain, that we know about with certain precision, is also related to interneuronal communication and with the receptor molecules of the neurotransmitters.

In order to communicate with other neurons, an elevated number of neurons in practically all regions of the brain release a transmitter, that while interacting with the corresponding receptor, produces a decrease in the excitability of these neurons. In other words it inhibits them. This inhibiting communication is so important that at this moment we recognize that many of the functions of the brain are correctly carried out thanks to the fact that the activity of millions of neurons is almost constantly decreased through such inhibition. Thus, it is not strange that the inhibiting neurotransmitter responsible for this has been the object of endless studies. Among the most important recent results of these studies is the understanding of the chemical structure of the receptor molecule which recognizes this transmitter, as well as the way it is found in the cavity of the neuronal membrane, and how the message is transferred so that the neuron is inhibited.

It is known that the receptor is a large and very complicated molecule with various places for chemical recognition that are oriented towards the exterior of the membrane of the neuron. One of these places recognizes the liberating transmitter by the neuron, so that when the message is transducted, the neuron is inhibited. But a different place recognizes, precisely, benzodiacepine, with the peculiarity that the result of the union of this drug to that place is the modification of the receptor in making it more sensitive to the transmitter. The final consequence is simple and surprising at the same time: when valium is present, the transmitter inhibiting neuronal activity is more efficient than when it is absent and thus, the neurons that recognize it are inhibited to a greater degree and anxiety is diminished.

The receptor is a large and very complicated molecule with various places for chemical recognition that are oriented towards the exterior of the neuron

Neurons, Chemistry and Mental Activity

Does this mean that there are neurons which cause anxiety and that when they are inhibited, this anxiety is lessened? Unfortunately we cannot yet respond in an affirmative sense to this question, nor in the case of depression that is corrected with the use of antidepressive drugs which also act by modifying interneuronal communication. The reason for our ignorance in this sense is that, in contrast with what happens in the experimental studies of plasticity-learning mentioned above, in which the number of types of neurons involved is very small (two or three), the brain functions responsible for "calmness" or for "emotional equilibrium", surely depend on the integrated functioning of hundreds or thousands of neuronal circuits, located in different regions of the brain.

Clearly this situation becomes even more complex if we refer to other functions that could be considered more mental in an anthropomorphic sense: conscience, intelligence, understanding of abstract concepts, creativity, imagination, the will, reasoning or sensitivity. At the moment, obviously, we cannot talk about neurons, circuits or neuronal networks, brain regions or neurotransmitters specifically responsible for these functions. But at the same time we cannot deny that neurons, circuits and neurotransmitters are the biological elements of mental activity.

To support the above affirmation let us go back to what we said in the introduction to this essay. Most psychotropic drugs, including those that produce hallucinations, alterations in perceptions, personality changes and symptoms similar to those of schizophrenia (such as paranoia and self-destruction), have a chemical structure similar to that of certain molecules which have been identified as neurotransmitters and that are capable of modifying interneuronal communication in some regions of the brain. We do not know, however, the manner in which these modifications are translated into the appearance of altered states of consciousness characteristic of those who are under the effect of such drugs.

This last sentence is an explicit acceptance of our total ignorance of the precise relation between brain biochemistry and mind. However, in recognizing our ignorance, we cannot escape the conclusion that the chemical phenomena responsible for interneuronal communication, participate in an important way in the mechanisms of mental functions. This is the only reasonable explanation for the amazing effects of psychotropic drugs. In the same way that epilepsy was for ages considered as a holy sickness, product of demon-like arts or as a divine punishment, and today no one with any culture believes in this type of explanation, so too it seems probable that future understanding will allow us to have a precise idea of the relation between brain chemistry and the mind.

Chemical phenomena responsible for interneuronal communication, are important participants in mental functions

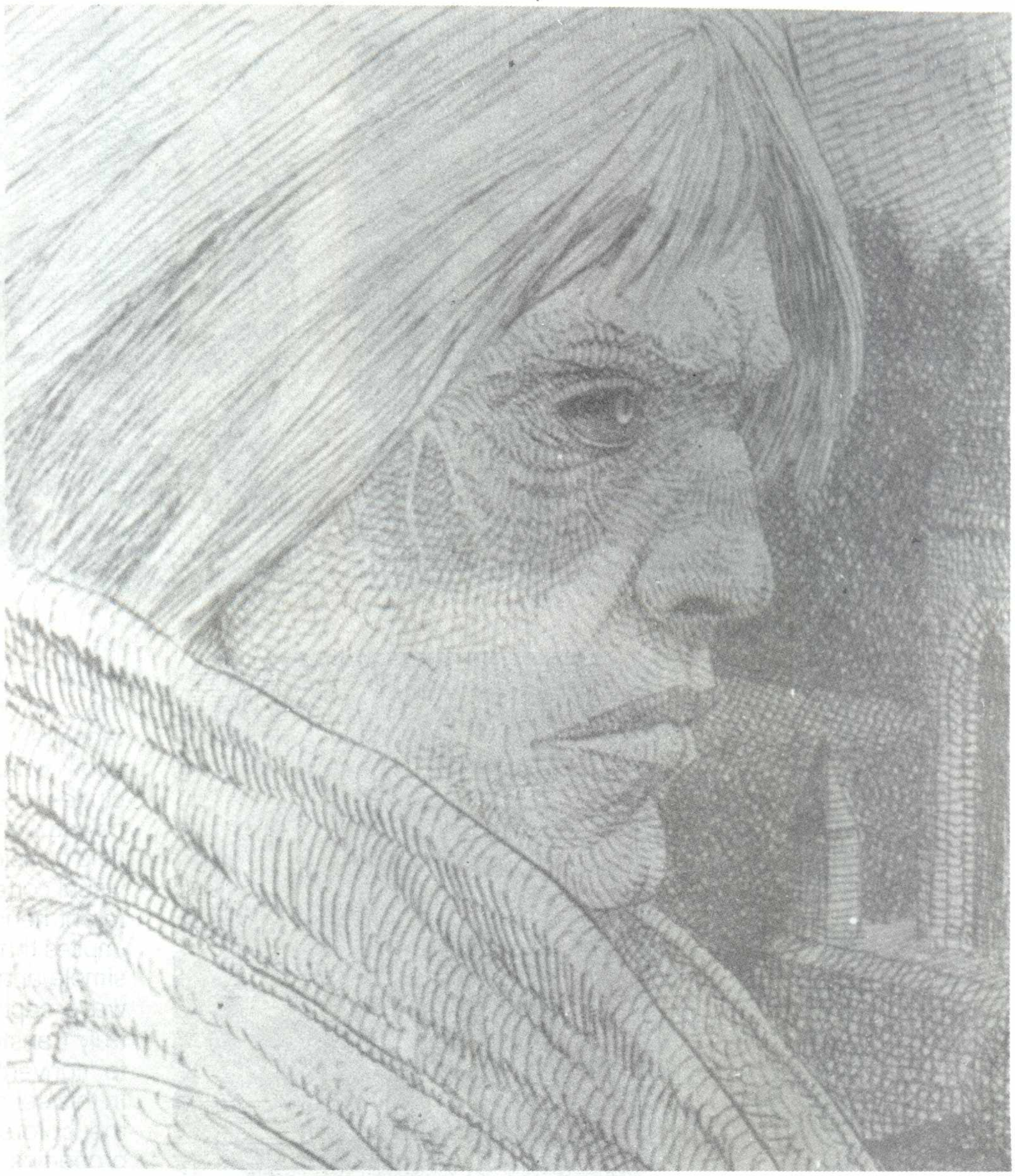
Let's consider, for example, the case of visual perception of colors. Recent research has shown that, though certainly the different photo-receptor cells present in the retina distinguish the length of the light waves they receive, what really allows us to identify color is the processing of information done by the neurons of the visual cerebral cortex (which is found very far from the retina, in the occipital region of the brain, the area where the

visual nervous tract ends). This processing, which occurs practically instantaneously –we do not have to "think" to know what color we are looking at– includes a comparison of the color perceived with the other colors present in the field of vision, and is done by the cerebral visual cortex through the activation of different neuronal groups. This mechanism implies that the brain does not carry out a simple analysis of the lengths of the light wave captured by the retina, but that it truly transforms the information received to "convert" it into the color we recognize. In this sense, the visual cortex re-creates the colors, according to the physical properties of the light emitted or reflected by the objects surrounding us.

We still don't know which neurotransmitters act in the process described above, but given that communication between neurons –in the visual tract as well as in any other neuronal circuit– uses the biochemical mechanisms mentioned before, it is clear that their participation is essential.

At this point we can speculate about how mental functions take place. Let us imagine that the extraordinary number of groups of neurons found in different regions of the brain, connected among themselves to form very complex circuits or networks –according to the genetic information which determines the multi-

It is clear that biochemical mechanisms are essential in communication between neurons

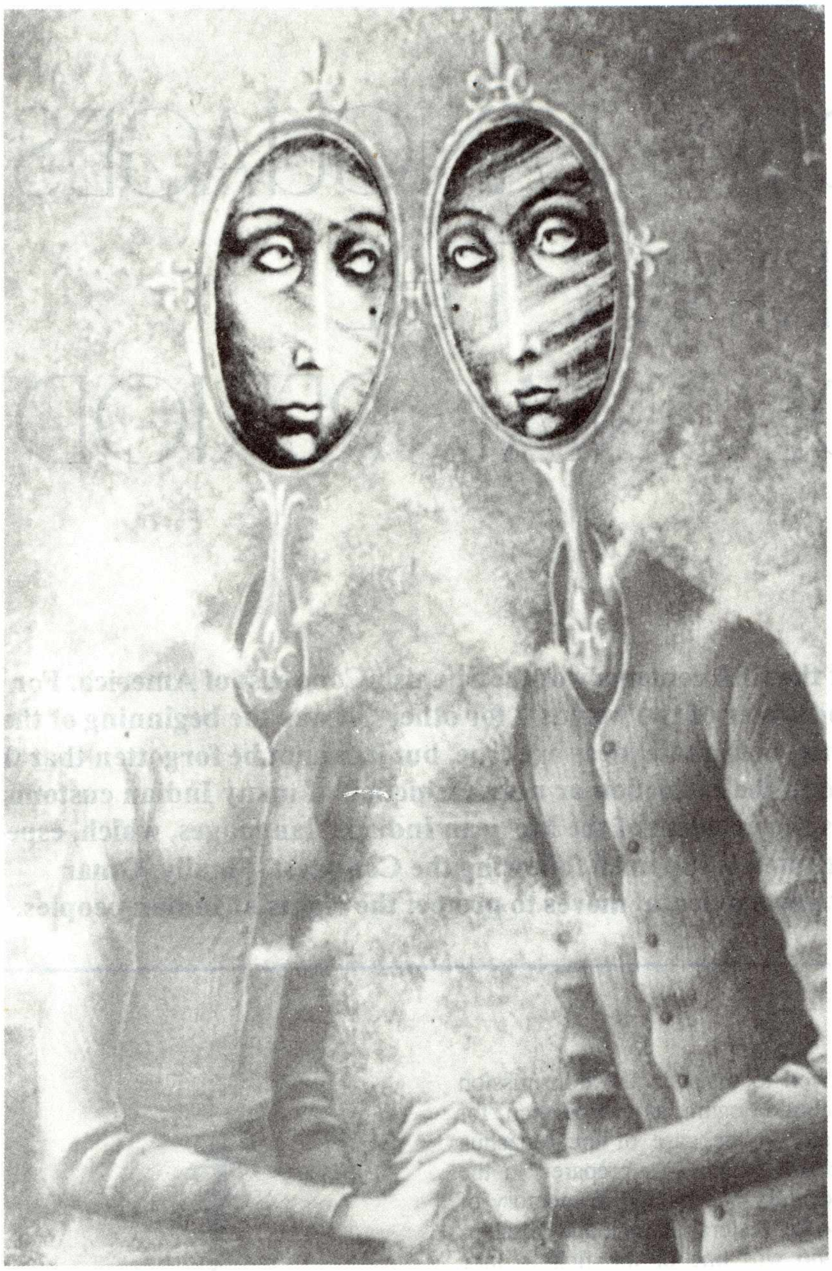


Drawing by Bilal. Reproduction by Alejandra Novoa

plication and differentiation of the nervous system– function analogically with the neuronal groups of the visual cortex, that upon processing the information coming to them from the retina, "create" the colors we perceive. Let's imagine for a moment that the information these groups and circuits are processing is not that which in a given moment is arriving from the outside world through the senses. It is, rather, information that has been stored in the form of short and long term memory through the phenomena of plasticity of neuronal communication from every-day experiences. The product of the unceasing processing would be mental activity. This of course would be changed when the functioning of interneuronal communication inside one or various circuits, is modified. Some examples of these modifications would be the action of psychotropic drugs, tranquilizers or antidepressants, brain traumas, and neuronal death caused by lack of irrigation of blood (cerebral embolism), by toxic substances or unknown causes in the case of Alzheimer'sdisease.

It is not surprising, given the complexity of the problem, that we are still far from knowing up to what point and in what way brain chemistry is responsible for mental functions. But let us recall the words of Thudichum, who in 1884 wrote the book *A Treatise on the Chemical Constitution of the Brain* "I believe it will be shown that the sicknesses of the brain and spinal medula are related to specific chemical

The biological problems most difficult to solve are those which have an almost infinitive number of plausible solutions



The Lovers, by Remedios Varo. Reproduction by Alejandra Novoa

changes in the neurons... In synthesis, it is probable that through chemistry, many alterations of the brain and of the mind, unknown today, may be defined with exactness and be sensitive to a precise treatment, and what is now the object of an anxious empiricism may be changed into the proud practice of exact sciences."

I think that if Thudichum had lived one century later, he would have been very happy to see how much things have progressed in the direction he pointed out. In this context we can cite an interesting idea of Crick, the co-discoverer of the double helix structure of Deoxiribonucleic Acid (DNA). In his recent book, *What Mad Pursuit*, Crick writes about his interest in neurosciences, and in referring specifically to the study of the mechanisms of consciousness he says: "Curiously, in Biology, it sometimes seems that the basic problems which appear impossible to solve, are the ones that are most easily deciphered. This happens because there can be so few and even remotely possible solutions, that finally one inexorably finds the correct answer. The biological problems truly difficult to solve are those which have an almost infinitive number of plausible solutions and one has to laboriously try to distinguish among them." Crick based this affirmation on his experience during the years he researched DNA, and though in my opinion he underestimated the complexity of the brain and its mental functions, I would certainly like him to be right. Time and our own human mind investigating itself will tell. ■

This article was first published by the magazine **Universidad de México,** #427, August 1990.