CURRENT CONCEPTS IN THE NEUROPHYSIOLOGY OF LEARNING

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Learning represents one of the most pervasive and fundamental biological processes observed throughout the animal scale. Although it is commonly accepted that learning implies the acquisition of information which tends to modify innate or already acquired performances of the organism, the great number of definitions proposed for this term reveals the difficulty in assessing the essential nature of the underlying mechanisms. The enduring changes produced by learning are usually associated with adaptive behavior. However, there are instances in which it may contribute to maladjustments of the individual.

Because of the ubiquity of learning in organisms of every grade of evolution, it seems warranted to conclude that it derives from a fundamental property of living matter, and that therefore, learning does not necessarily require special complex neuronal circuits. In order to designate that property we have adopted the term plasticity proposed by Konorski (1948), thus establishing its distinctiveness from another fundamental property of living cells, excitabiltty, which is related to very transient and reversible changes produced by the stimulus. Granting that through specialization of function, plasticity as well as excitability developed more in certain elements of multicellular organisms, there is no doubt that the nervous system is endowed with the privilege of both properties. In animals with nervous systems in which "all or none" signals are transmitted, plasticity permits the storage of information delivered by those signals, whereas excitability is concerned with their generation and transmission. Furthermore, it seems obvious that through the evolution of the nervous system, some neurons developed longer and more excitable axons for transmission than other short-axon non-propagating elements. From the observation that the former type of neurons do not present enduring plastic changes upon stimulation whereas the latter are essential for those changes, the hypothesis of an evolutionary differentiation of excitable and plastic neurons within the central nervous system

(C.N.S.) may be safely conjectured.

Since nothing is known about the ultimate nature of plasticity, our knowledge on the neural plastic changes associated with learning derives mainly from the indirect changes of excitabiltiy currently assessed by electrophysiological techniques.

For discussion of the main neurophysiological correlates of learning it is necessary to establish a general classification of the fundamental types observed from Protozoa to man. First of all, learning may be divided into negative and positive. While negative learning leads to decrement or disappearance of a response previously evoked by a given stimulus, positive learning involves the acquisition of a response to a stimulus which did not elicit it before. The elimination of irrelevant responses during negative learning is not a passive phenomenon but depends from central processes actually preventing their appearance which otherwise would occur. These active restraining influences have been termed "plastic inhibition" in order to distinguish it from Sherringtonian transient inhibition. On the other hand, the acquisition or enhancement of responses during positive learning requires the establishment or facilitation of neural connections by a process designated "plastic association" in this modern terminology. Plastic inhibition is probably the primary and most important process in learning without which animal behavior would be disorganized, and adaptation of the organism to the external environment would be impossible. Plastic inhibition is so important for normal functioning of the central nervous system that it may not be exaggerated to say that while plastic inhibition may develop in the absence of plastic association, the latter is always accompanied by the former.

According to their complexity, the following types of learning may be considered: a) habituation; b) classical conditioning; c) instrumental conditioning or trial and success learning; d) latent learning. Besides, a separate variety of learning produced by a single exposure to a stimulus in newborn

animals of certain species and termed imprinting may be added.

A number of neurophysiological studies carried out during the last decade have contributed to an initial understanding of the functional role of various brain regions in certain types of learning.

Habituation.- Habituation, which represents the simplest type of learning, consists in an enduring, progressively oscillating decrement of responses produced by monotonous repetition of a stimulus which loses significance for the organism. This pervasive phenomenon is observed not only in effector responses but also in sensory experiences as everybody can confirm in everyday life. A logical question to ask is: what changes occur in the C.N.S. during habituation which may account for all its manifestations? Recordings of the electrical activity of the neuroaxis in unrestrained animals with electrodes permanently implanted have disclosed neural correlates of habituation both at the specific and at polisensory systems in the brain and spinal cord. The terms "afferent neuronal habituation" and "neuropil habituation" have been proposed for designating each process respectively.

Neuropil habituation is accompanied by decreased excitability of the neural pathways where impulses of various sense modalities converge. This has been shown by recording the background or ongoing activity of the brain, as well as the activity evoked by brief sensory or electrical stimuli. Indeed, by monotonous repetition of a stimulus, the originally diffuse evoked potentials diminish in amplitude and tend to remain restricted to the specific afferent pathways. But if the intermittent rhythmic stimulation is prolonged enough, blocking of sensory transmission can be observed within the specific afferent pathway itself. This phenomenon called afferent neuronal habituation is first seen at the cortex and it later extends down to the first sensory synapse and to pre-receptor mechanisms which are known to reduce the intensity of sensory stimuli before impinging upon sensory receptors.

Perhaps the most basic manifestation of neuropil habituation is that

concerned with the arousal reaction. In this regard, it is interesting to point out that monotonous repetition of a stimulus which at the first presentation elicits a prolonged EEG desynchronization, not only tends to produce progressively shorter arousal reactions until its disappearance, but subsequent presentations of the same stimulus elicit the EEG synchronization characteristic of the initial stage of sleep.

Based on the available evidence, the following neurophysiological mechanisms may be proposed in order to account for the various manifestations of habituation.

1. Sensory or non-sensory activation of neurons within the diffuse polysensory pathways extending throughout all the levels of the central nervous system tend to produce recurrent inhibition of the same neurons, possibly by short collateral circuits involving inhibitory interneurons.

2. Rhythmic sensory stimulation elicits a progressive recruitment of hypnogenic neurons along a recently disclosed "sleep system" which in turn inhibit the arousing neurons of the "vigilance system".

3. Prolonged repetition of non-significant stimuli activate inhibitory mechanisms at the brain stem which partially block the entrance of afferent signals to the C.N.S. ("sensory filtering"). Independently, centrifugal mechanisms acting upon peripheral pre-receptor effects reduce the intensity of sensory stimuli.

Classical conditioning. The work of the russian school created by Pavlov has established that by adequate timed pairing of an indifferent stimulus with another one eliciting various somatic or autonomic responses (unconditional stimulus, US), the former one (conditional stimulus, CS) acquires the capacity to elicit similar responses (conditioned responses, CR). When studying the effects of this procedure it becomes evident that the earliest conditioned

responses are elicited by the environmental stimuli associated with the US. It is only after most of those conditioned responses to the environment become extinguished that the animal learns to respond selectively to the experimental CS. Two different processes are obviously involved in this sequence of events which lead to the following basic question: Which is the locus of the plastic association responsible of the acquisition of conditioned responses? Which are the neural events underlying selectivity of a given conditioned response and extinction of irrelevant responses?

Contrary to classical Pavlovian assumptions it has been demonstrated that ablation of the "cortical analyzers" and even total ablation of the neocortex does not prevent conditioning. On the other hand, small subcortical lesions at the midbrain level seriously interfere with the earliest plastic associative changes of conditioning. These observations emphasizing the neglected importance of subcortical structures in conditioning and learning have been supported by data derived from modern electrophysiological techniques. Indeed, electrical recordings from the brain of animals during classical conditioning have revealed the following changes: a) a generalized neocortical EEG desynchronization which appears prior to the behavioral conditioned response; b) during this early phase the potentials evoked by the CS appear widespread throughout the polysensory system and can be recorded all over the cortex and from numerous subcortical structures; however, the earliest increase of excitability has been detected at the mesencephalic reticular formation both by the appearance of conditioned specific frequency responses and by a significant reduction of the recovery cycle of reticular evoked potentials; c) a rhythmic theta rhythm 4-6 c.p.s. appears in the hippocampus and entorhinal cortex simultaneously with the orienting reaction; d) the initially generalized EEG neocortical desynchronization and the enhanced potentials evoked by the CS become localized to the cortical area corresponding to the specific afferent pathway activated by the US; e) the hippocampal response disappears

in later stages of conditioning. Microelectrode recordings performed during conditioning. have confirmed and extended the studies of macropotentials. In fact, polyvalent units in the reticular formation were most readily affected by conditioning, and at the stage of localized desynchronization, the CS affected only the corresponding cortical neurons as well as some thalamic neurons which were unresponsive prior to conditioning.

All the abovementioned observations provide experimental basis for the following interpretations:

1.- The polysensory system and not the specific afferent systems or Pavlovian analyzers play a fundamental role in plastic association during conditioning.

2.- The earliest plastic associative changes appear to occur at the level of the mesencephalic reticular formation. This should not be surprising considering the essential participation of that brain stem region for arousal and alertness as demonstrated by Magoun and his associates.

3.- While the cerebral cortex is not necessary for plastic association during the earliest phase of conditioning, the integrity of the mesencephalic reticular formation is essential at this time.

4.- Polyvalent reticular units responding to several sensory modalities seem to be particularly important in forming the initial connections.

5.- The early dominance of the mesencephalic reticular formation is later shifted to thalamic levels allowing more selective cortical effects.

6.- At this stage, the hippocampal system becomes activated and possibly influences the reticular formation by inhibitory interaction.

As it will be discussed below, it is not far-fetched to assume that the hippocampal formation plays an important role in the integration of present and recently past experiences.

The plasticity of the cerebral cortex has been demonstrated by studies with direct current polarization. Conditioning to a tone has been shown to occur when anodal polarization is applied to the motor cortex; and interference in performance of a motor CR to a flicker has been observed during and after negative polarization at the visual cortex. Furthermore, a chronically isolated cortical slab displays specific rhythms of a stimulus applied during polarization when a stimulus of another frequency is presented.

By the same token, there are studies indicating habituation and plastic facilitation in the isolated spinal cord.

It may be concluded that there are plastic neurons at all the levels of the C.N.S. from the spinal cord up to the cortex.

Internal inhibition. When the conditional stimulus is repeated without reinforcement the conditioned response is extinguished. Electrophysiological recordings have shown that the EEG and the conditioned evoked potentials present similar changes during extinction and habituation. During extinction, differentiation, delayed inhibition and supramaximal inhibition the negative conditional stimulus acquires cortical synchronizing properties. This may be the result of different degrees of activation of the hypnogenic system. Just as changes in the electrical activity of the brain are detected before the behavioral conditioned response appears, during extinction those changes persist beyond the disappearance of the behavioral response.

External inhibition. Blocking of a conditioned response produced by an alerting novel stimulus is accompanied by EEG desynchronization and reduction of the evoked potentials related to the conditional stimulus both in polysensory structures and in the specific afferent pathways as far down as the first sensory synapse. Therefore, external inhibition may be identified with distraction from the conditional stimulus and all its associated neurophysiological mechanisms.

<u>Instrumental conditioning</u>. This term is used to designate a training procedure by which the animal learns to perform an arbitrarily selected behavioral response normally present in its repertoire followed by a reinforcing or rewarding situation consisting either by satisfying needs for food or water, or by terminating or preventing a noxious stimulus. In this type of learning, performance of the conditioned somatic response alters the external environment and is "instrumental" in achieving the motivational goal of the organism. So far, no visceral responses have been conditioned by this procedure. If somatic instrumentally conditioned responses are dependent from the central mechanisms involved in voluntary behavior as it is usually assumed, it would be doubtful that autonomic responses might be instrumentally conditioned.

During the early phase of experimental instrumental conditioning the animal performs a series of unsuccessful trials until the correct performance is fully aprehended. That is why this type of learning has also been termed "trial and error". In any case, the term "trial and success" seems more correct because the animal learns by success and not by error.

Many tasks of different complexities have been devised by experimental psychologists using the fundamental principle of instrumental conditioning, and the effects of localizedcortical ablations on acquisition, retention and performance have been studied. More recently, it has been found that subcortical lesions in several limbic regions such as the hippocampus, the amygdaloid complex and the septum interfere with some aspects of the learning processes. Unequivocal interpretations of the results can hardly be obtained because of the multiple factors involved.

Attentional and motivational factors certainly play an important role in facilitating the corresponding plastic associations. Reserving attention for a later discussion, it can be stated that while motivation is essential

for the acquisition of instrumental conditioned behavior, it is unnecessary for establishing classical conditioned responses. This has been shown in conditioning produced by using direct electrical stimulation of the cerebral cortex as CS and US. However, motivation tends to facilitate that simple plastic association by lowering the threshold of the sufficient CS. The work of Olds concerned with self-stimulation of the brain has indicated the important participation of subcortical limbic and mesodiencephalic structures for positive and negative reinforcement, respectively.

Electrophysiological studies of instrumental conditioning made in recent years have demonstrated significant changes in widespread structures of the polysensory system during this type of learning. For instance, with the initiation of avoidance conditioning to flickering light, a marked increase in frequency specific activity occurs in visual and auditory cortex, reticular formation, superior colliculus and lateral geniculate but not in amygdala, hippocampus and n. ventralis anterior of the thalamus. Early in conditioning the hippocampus begins to respond, and later the specific frequency responses appear in n. ventralis anterior. Therefore, it is evident that a particular sequence of events in different neural structures occur with temporal development of learning. It is interesting to note that in differential approach-avoidance conditioning the frequency of the electrical responses in the specific and polysensory systems correspond to that of the C.S. when the behavioral response is correct, whereas during incorrect performances the frequency of the electrical responses in the polysensory structures corresponds to that of the C.S. for which the behavioral response would have been correct. Other experiments support the view that changes of macropotentials as those mentioned above are related to processing of signal-derived information by these structures. The introduction of average response computation and signal analysis methods have recently permitted the study of waveshape detail during

instrumental conditioning. In brief, it has been found that as informational significance is attached to conditional stimuli, the corresponding evoked potentials in widespread regions of the brain become highly similar in waveshape. These data support the view that learning involves the formation of anatomically extensive functional circuits in which several levels of the brain are temporally coordinated in a highly specific fashion.

Latent learning. This term has been used to denote learning without patent reward. Actually, the information derived from latent learning is inclusive within the common term memory. The neurophysiological problem of memory and its associated consolidation process cannot be divorciated from the antecedent carrying information process. In this regard, there is no doubt that stimuli better attended to leave more stable and accessible memory tracings than those present out of the span of attention. Recent studies in humans in whom averaged evoked potentials were correlated with task performances have shown a strict parallelism between the size of the potentials and the performance efficiency. The most significant changes occur in the late components of the evoked potentials corresponding to activation of the polysensory system. It is now established that the brain possesses a filtering mechanism which selectively facilitates and inhibits the entrance of sensory signals to the C.N.S. during attention, and that the signals which by-passed the filter require the integrity of polysensory structures in the brain stem for "conscious integration". But besides the information consciously perceived and stored in the brain there are indications that a great amount of information of which the individual is not aware of also leaves memory tracings which can only be retrieved in special circumstances such as dreaming or hypnosis. The confirmed observation that the content of dreams and hallucinations is made up of memory tracings released in those conditions leads to the question of possible inhibitory influences acting upon mnemic neurons during ordinary wakefulness. If this hypothesis is true, it may open an avenue of research

for the scientific study and application of drugs capable of enhancing memory and mnesic associations. On the other hand, a better understanding of the neurophysiological mechanisms of attention may find a practical application for increasing the brain capacity to receive selective information. Hopefully, investigation along these lines may prove fruitful in the scale of mental activity from mental retardation to creative thinking.