as suggested by HERNÁNDEZ-PEÓN[7] although there was no indication that doses even approaching anaesthetic level induced any change other than a reduction. The effect of chlorpromazine is apparently an all or none phenomenon, not a graded one. The decrement of auditory evoked potentials following the administration of this drug is probably correlated to the state of behavioural indifference induced by chlorpromazine and is in agreement with the various suggestions[1,2,4] that its action may be upon mechanisms concerned with the modulation of sensory inflow.

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EVOKED POTENTIALS AND VISUAL INFORMATION PROCESSING UNDER THE ACTION OF PSILOCYBIN IN THE CAT

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During the study of visual evoked potentials in a series of human volunteers submitted to the action of a hallucinogenic drug (psilocybin) with the aim of investigating the alterations in the processing of visual information, simultaneous with the hallucinations, the problem of the variability of the results forced us to precede these tests with a series of animal experiments.

In order to determine the action of hallucinogenic drugs on sensorial mechanisms, it seemed necessary to us to differentiate between the alterations that are effectively the direct result of the modifications occurring at different levels in the visual system, and those alterations that the drug provokes on other sensory modalities, on vegeta-

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tive mechanisms or on the mechanisms controlling the emotions, on the mechanisms of attention and unspecific activation of the brain.

In view of the existence of complex specific and non-specific mechanisms of convergence, there can be an indirect action on the visual system through these mechanisms.

We have done three series of experiments: (*1*) in intact animals with implanted electrodes (chronic preparations), (*2*) in unanaesthetized animals (the *encéphale isolé* preparation), (*3*) in unanaesthetized preparations immobilized with Flaxedil, with simultaneous observation of arterial tension in four cases, through a catheter introduced into the femoral artery, connected to a pressure transducer.

In the interpretation of the results we think that evoked potentials represent so complex a process that the observed modifications cannot adequately be described in terms of facilitation or activation in the case with higher amplitude and inhibition where a diminution is observed.

We think that a first approach to the problem of hallucinations can be attempted through the consideration of the intermediary phases of information processing, of which man is not conscious.

METHODS

Six acute experiments were performed with the *encéphale isolé* cat preparation; ten experiments with four chronic cat preparations with considerable restriction of movement through the use of a restraint system, and five acute experiments in cat preparations immobilized with Flaxedil.

Visual evoked potentials were recorded in the G. marginalis, G. suprasylvius and G. ectosylvius. In the chronic preparations, the electrodes were bipolar, the distance between them being approximately 2 mm. In the acute experiments the reference electrode was placed on the neck muscles and after cranial trepanation and opening of the dura, the electrodes were placed in direct contact with the pia mater.

No recording was done under anaesthesia. After tracheotomy the cats in the acute experiments were maintained by artificial respiration.

Recording was done through an AC-coupled conventional amplification system formed by Tektronix 122 low-level preamplifiers and by Tektronix 502 and 561 oscilloscopes, on which the potentials were photographed. The visual stimulus consisted of the light from a 500-W Tungsten lamp of a projector with intermittent interruption of the light beam with an electromagnetic screen controlled by a Grass S4 Stimulator, the impulses from which were 0.001 V and 100 msec duration and were amplified by an EEG apparatus.

Psilocybin was administered in doses of approximately 150 μg/kg, intraperitoneally, except in the *encéphale isolé* preparation in which case the same dose was given intramuscularly followed after 45 min by the same dose intravenously administered.

In the chronic cat preparations, recordings were done in a sound-proofed box.

RESULTS

Visual evoked potentials were observed not only in the primary visual area but also in the visual association area and in the primary acoustic area, both in the acute and in the chronic preparations (the latter with bipolar recording).

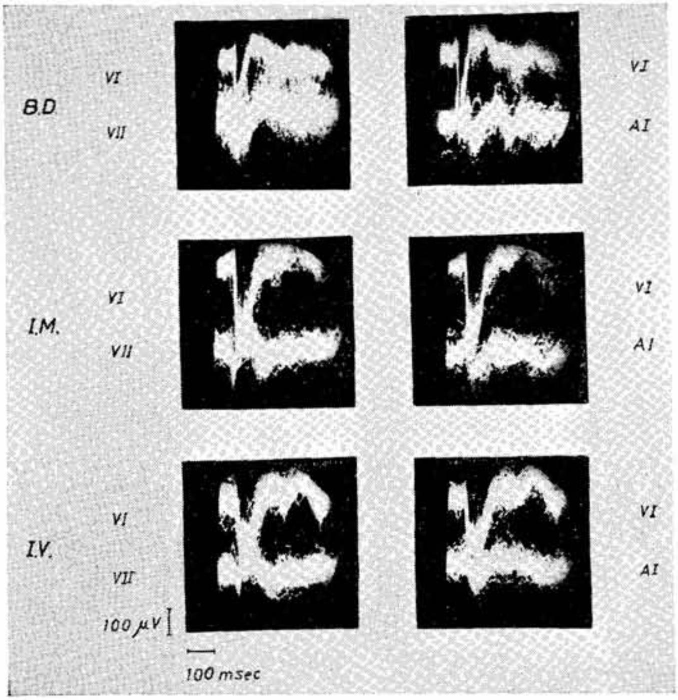

Fig. 1. Effect of psilocybin on visual evoked potentials, recorded in VI and VII in an *encéphale isolé* preparation. B.D. Recordings done before the administration of the drug. I.M. Recordings done after intramuscular administration of the drug. I.V. Recordings done after intravenous administration of the drug.

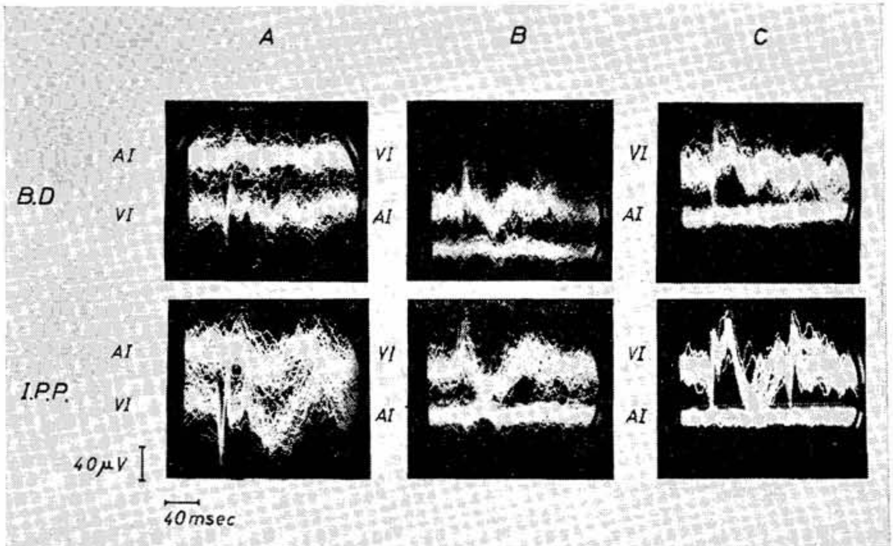

Fig. 2. Bipolar recordings of visual evoked potentials in chronic preparations, in areas VI and AI in a sound-proofed box. B.D. Before intraperitoneal administration of psilocybin. I.P.P. After intraperitoneal administration of psilocybin in three different animals (A, B & C).

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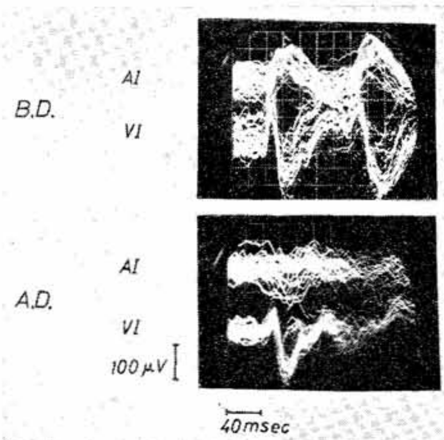

Fig. 3. Recordings of visual evoked potentials in a Flaxedil-immobilised preparation. B. D. Before intraperitoneal administration of psilocybin. A.D. After intraperitoneal administration of psilocybin.

In the acute experiments with the *encéphale isolé* preparation, after intramuscular administration of the drug, there was no modification of the latency of the first positive wave. The amplitude was not markedly changed although a small reduction was observed. There was a very clear modification to the duration both of the first positive and second negative waves. Both waves had a smaller slope and their peak was attained later.

After intravenous administration of the drug the diminution in amplitude showed a clear accentuation but the latency remained unchanged (Fig. 1).

In the chronic cat preparations the latencies did not show any modification but the amplitude and the duration of the first positive and second negative waves were greater in every case (Fig. 2). In the unanaesthetized cats immobilized with Flaxedil, the modifications were a reduction in amplitude as in the *encéphale isolé* after intravenous administration, although less intense (Fig. 3).

After administration of psilocybin the arterial pressure showed increases of short duration. Spontaneous recordings of electrocorticography carried out in the sound-proofed box, completely dark and without any stimulation, were mostly of a desynchronized type after psilocybin, although in some cases there were no changes.

DISCUSSION

It can be seen that, in a situation similar to that in which hallucinations occur in man, psilocybin produced marked modifications of visual evoked potentials in the cat.

Results with chronic preparations were similar to those reported by PURPURA[6] in cat chronic preparations with LSD 25, and those obtained with the *encéphale isolé* and Flaxedil preparation are in some respects in agreement with the findings of EVARTS[1] with LSD 25 in the *cerveau isolé* preparation under anaesthesia.

As the evoked potentials represent the activity of nerve cells, it is reasonable to conclude from their modification that in this situation there is an alteration in visual information processing. This difference could be due to an effect on cell metabolism or to a change in the patterning of the nerve cell interactions[3,5].

Our viewpoint in the study of evoked potentials was to consider these potentials as (*1*) phenomena that represent electrical correlates of physiological mechanisms, but at the same time, (*2*) signals that carry a quantity of information. The drug acts on the physiological processes, but an alteration in the amount of information (in the sense of the mathematical theory of communication[8]) and probably also of the semantic content of the message, must result from the modification of the signals.

The greatest difficulty in our study comes from our ignorance of what the evoked potentials represent. They are the result of sensory afferent signals arriving at the cerebral cortex and being transmitted transcortically, but we do not know the level of integration of the process, and correspondingly we ignore the level of processing of information. The modification of evoked potentials that we have observed occurred not only in the primary visual area but also in the association and in the acoustic primary area.

It seems that there is a dissociation between the more intense modification in the primary visual area, and the modification in the associative area (G. suprasylv.) and in the acoustic primary area (G. ectosylv.) which, except in one case, were much more discrete. The fact that there are visual afferent potentials in the acoustic area and different modification of the evoked potentials in these areas, as compared with the visual primary area is interesting because it suggests a confirmation of the classical idea that in hallucinations the interaction between the different sensory modalities may be an important factor.

Since it is known that the action of selection and filtering of the afferent information is performed by the reticular system, and as in our experiments the phenomenon of arousal, and variations in amplitude of the evoked potentials were observed to be greater in some areas than in others, we must admit the participation of the mechanisms dependant on this system, in our results. The association of multisensorial systems must also be considered in the explanation of the modification of visual evoked potentials in association areas and in the acoustic primary area.

Psilocybin has such a complicated action on the central nervous system that we must also consider the possible influence of modifications of central vegetative mechanisms, for instance the variation in the arterial pressure may have been of considerable importance in our animal experiments.

Summarizing our views, we can say that visual information is processed at different levels in the nervous system—visual system, reticular system, association systems, vegetative system, and among the operations that occur in the cerebral cortex we must consider a processing of "cognitive level". It is reasonable to consider in this context the cognitive mechanisms as implying a processing of information similar to those proposed by PITTS AND MCCULLOCH[4,2] or by RASCHEWSKY[7] for the recognition of Gestalts.

At the cognitive level there could be, as in electronic computers, an ambiguity in the signal considered (*1*) as a certain content upon which operations are done and (*2*) the signal meaning rules and instructions of operation upon this content, these signals being integrated in an adequate programme.

There is indirect evidence that evoked potentials may correspond not only to an

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elementary sensory processing, but result from action that includes a process of cognitive order as is suggested by the studies of unitary responses in the retina, nucleus geniculatum laterale and in the cerebral cortex, that aim at the conclusion that there occur processes implying the extraction of Gestalts, what is already a cognitive process. Although the evidence is indirect, this basis can be used in the construction of models of the phenomenon, sufficient to describe the situation (although not necessarily existent in this form).

One of the aims of such a study would be to examine the possibility of establishing a number of operational hypotheses to serve as a basis for the concept of psychophysical relationships which are essential to the understanding of hallucinations.

It is possible that evoked potentials represent global results of processes which include all levels of integration. With the data from all these levels, a neuronal model

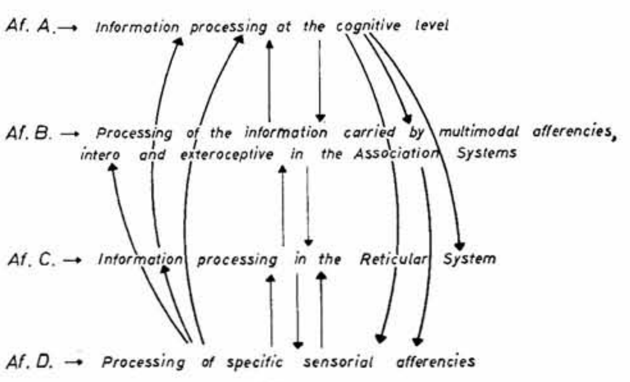

Fig. 4.

of the outside world would be formed in the CNS. These data would be included in a redundant fashion in different categories and would represent interaction between different levels of organisation. For example, in hallucinations the perception process would be modified from the higher cognitive level to the more elementary one (Fig. 4). Thus the hallucinogenic drug would modify the information processing in each category at different stages, and the interaction of different types of process. Thus elementary processes already modified could be integrated in cognitive processes different from those with which they are usually correlated, and the same thing could occur at different levels of integration (Fig. 5).

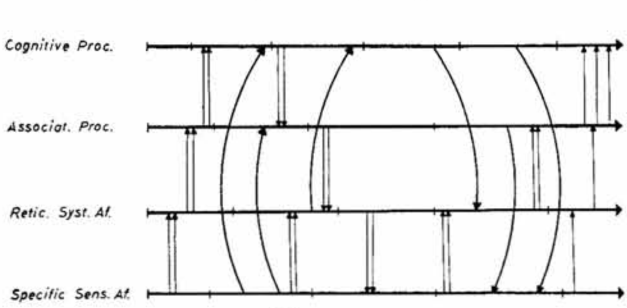

Fig. 5.

Global processes would be modified and hallucinations would arise from the emergence of the result of a different information process occurring, from the psychological viewpoint, as an unconscious process, and in which the intermediary levels of processing could be of decisive importance.

Whether the individual is convinced or not of the true quality of his false perception would depend on other, and more global, alterations—as those that are possibly behind the schizophrenic "erleben" but do not exist in the epileptic aura or in the great majority of individuals under the action of hallucinogens.

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NEUROPHYSIOLOGICAL AND PSYCHOLOGICAL STUDY OF PSILOCYBIN-INDUCED MODIFICATIONS OF VISUAL INFORMATION PROCESSING IN MAN

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In our series of experiments in the cat, with a dose of psilocybin identical to that used in man, very consistent modifications of evoked potentials appeared in each type of preparation.

With regard to the study of evoked potentials in man, we would like to show some results that allow us a partial formulation of the problem. The aim of our study was to observe some modifications of visual information processing during the action of psilocybin, which express themselves in neurophysiological data, and search for possible correlations with the level of the Critical Flicker Fusion Frequency, (CFFF), results of Benton's Visual Retention Test, and protocolled subjective and behavioural data, obtained from normal volunteers. We were specially interested in the cognitive processes, which we first examined by means of Benton's Test.