THE ASSESSMENT OF PAIN PERCEPTION.

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THE assessment of pain perception is a subject of great importance from both the practical and the theoretical aspect. The increasing use of curare-like drugs as muscular relaxants and basal anaesthetics (Mushin, 1951), and in conjunction with electro-convulsant therapy (E.C.T.), has made the orthodox tests for depth of anaesthesia unreliable because they depend on the activity of voluntary muscle. E.C.T. itself (Morgan, 1950) and industrial electrical accidents (Hume, 1935) have given rise to unusual states of consciousness which cannot be fully understood until more is known about the way in which electric shock affects the central nervous system. On the theoretical side many explanations of the essential features of a state of consciousness have been given, but none of them accounts completely for all the observed phenomena ; investigations designed to improve methods of assessment should provide useful information which, when correlated with that from other fields, may ultimately lead to a better understanding of the conscious state. The object of the experiments described in this paper has been the development of tests which will indicate the level of consciousness, and in particular the appreciation of pain, when the voluntary muscles are paralysed.

EXPERIMENTAL METHODS.

Material.—The material consisted of—

(i) Rabbits of both sexes of various breeds and ages, ranging in body weight from 800 gm. to 2,000 gm.

(ii) Six normal male human subjects ; 5 mental hospital patients, male and female, classified as depressive.

Apparatus.—Electro-cortigrams (E.Co.G.) were recorded on a 6-channel Mitchell E.E.G. machine and on a Marconi 4-channel machine ; heart rates were recorded by taking electro-cardiograms on one channel of the E.E.G. machine. The electrodes for the animal E.Co.Gs. consisted of fine stainless steel pins driven through a cork support and the skull of the anaesthetized animal so that the tips of the pins were in contact with the cortex. The penetration of the pin was checked *in vivo* by X-ray, and post-mortem by histological methods (Marshall, 1940). If the cork support was sutured to the skin over the skull, the electrodes could be left in position for several days without apparent discomfort (Fig. 2). These electrodes were used for E.Co.G. recordings and for stimulation ; they were connected to the required leads by crocodile clips. Three standard positions were used, the external landmarks being—

(i) the level of the posterior canthus of the eyes ;
(ii) midway between (i) and the anterior border of the base of the ear ;
(iii) the level of the anterior border of the base of the ear.

Hypodermic needles were used as electrodes for recording the animal electrocardiograms ; they were placed subcutaneously, one over the heart and the other over the lumbar vertebrae (or on any other accessible " indifferent " site).

The electrodes for the human E.E.Gs. were the usual Marconi scalp type, and were placed on the occipital and parietal areas. Human electrocardiograms were recorded on the E.E.G. machine with scalp electrodes placed over the heart and on the left arm.

The stimulator used for the rabbit experiments was modelled on that described by Bernstein (1950) and was designed to provide a constant current and square wave pulses. The pain stimulus for the rabbit was a pin-prick on the nose, and in the experiments with human subjects 0·1 ml. distilled water was injected intradermally on the forearm.

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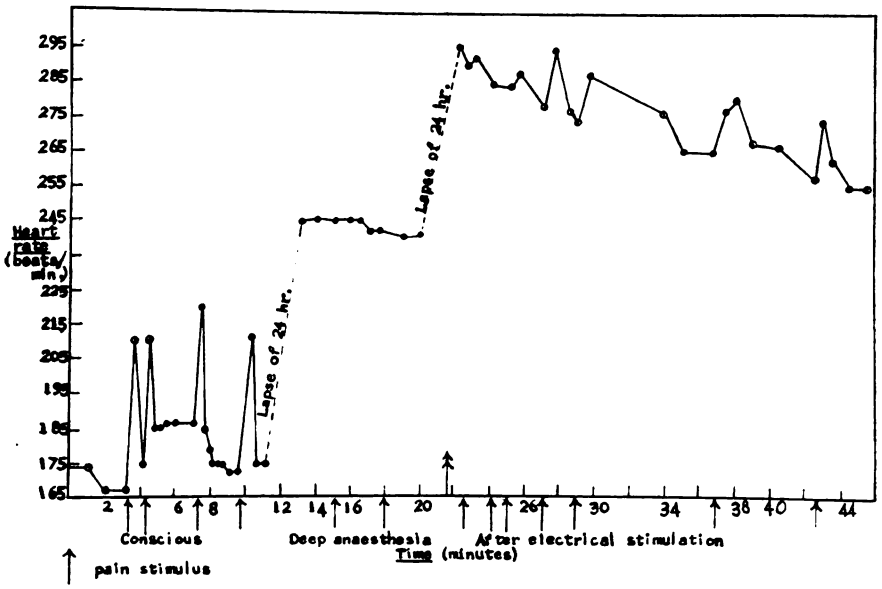


FIG. 1.—Arrangement of electrodes for rabbit recordings and stimulation.

RESULTS.

The results will be described under two main headings:

(1) Determination of sensitivity to pain by the cardiac pain reflex (c.p.r.).
(2) Assessment of level of consciousness by E.Co.G. and E.E.G.

Determination of Sensitivity to Pain by Cardiac Pain Reflex.

In order to assess the awareness of the animal under these conditions it was necessary to use involuntary muscle, under cerebro-cortical control, the activity of which could be easily recorded. Longley suggested that the cardiac muscle fulfilled these conditions, and the electro-cardiogram was recorded on the E.E.G. machine concurrently with the E.E.G. itself.

The normal heart-rate of the rabbit varies from 190–290 beats/minute, but in any particular animal the resting rate only varies by 1–2 per cent. from the mean value. When the conscious animal felt pain, in the form of a pin-prick on the nose, the heart-rate increased by 20–30 per cent.; typically the increase lasted about 15 seconds, after which the rate quickly returned to the resting level, or to a subnormal level for a few seconds. The response always occurred and its magnitude was fairly constant in any one animal, varying little with the strength of the stimulus. When the animal was deeply anaesthetized the response was completely abolished, and in states of light anaesthesia it was reduced in magnitude, and the return to normal was slower (Fig. 2). The cardiac pain reflex behaved similarly in human subjects tested in the conscious state and at various levels of ether anaesthesia.

In the rabbit, immediately after an electrical convulsion, the c.p.r. was absent, and the stage at which it could first be elicited is shown in Table I. The reflex invariably appeared before the paw retraction reflex, and was in fact present at a time when the animal would normally be considered unconscious; voluntary movements appeared some minutes later (Table I). In human subjects there was a stage, just before consciousness was lost, when the c.p.r. was positive but no other external indication of pain perception was given; subsequent interrogation revealed that the subject felt the stimulus, but "had no energy to signal."

Assessment of Level of Consciousness by E.Co.G. and E.E.G.

The normal conscious E.Co.G. from the precentral granular area of the rabbit cortex has a characteristic 5–8 cyc./sec. rhythm, while that from other parts of

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TABLE I.—*Reappearance of Reflexes after Electro-convulsant Stimulation (Rabbit).*

No.	*Conscious.*	*Cardiac pain reflex. After electrical stimulation.*		*Paw reflex.*
	Per cent. increase in heart rate.	Time when first seen (minutes after stimulation).	Per cent. increase in heart rate at this time.	Time when first seen (minutes after stimulation).
1	11	2¼	7	6
2	26	3	4	6
3	40	2	6	4
4	10	2½	5	7
5	11	5	1	9
6	—	3	4	5
7	25	4	13	
8	6	5	2	
9	15	4	7	
10	12	5	7	
11	12	5	10	
12	—	4	10	

The c.p.r. was tested every minute in all experiments until a positive response occurred. The paw reflex was not timed accurately in rabbits 7–12, but it was never present at the time when the c.p.r. appeared.

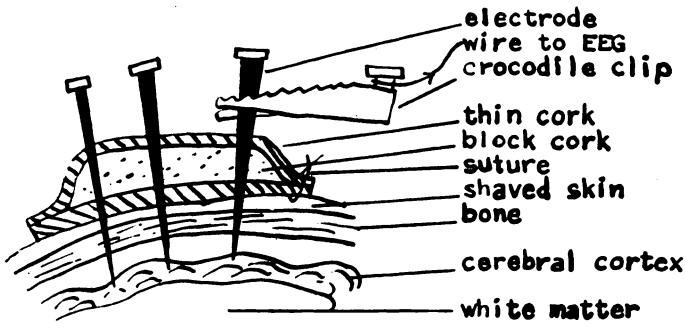


FIG. 2.—Effect of pain stimulus on rabbit heart rate under different conditions.

the cortex is less regular, but always contains a high proportion of fast rhythms; slow frequencies, as in man, are indicative of decreased cortical activity, or of a pathological condition. A number of E.Co.Gs. of rabbits in different stages of Nembutal and Pentothal anaesthesia were taken, and the changes in the record agreed reasonably well with the observed state of the animal.

In the human subject the α-rhythm was recorded while the depth of ether anaesthesia was gradually increased. The percentage of E.E.G. record showing no α-rhythm was calculated for each 20-second period, and a sharp rise in this percentage occurred, as unconsciousness supervened, in every one of six subjects tested (Fig. 3).

E.Co.G. recordings could be made 1 second after switching off the current used for electric shock in the rabbit. At the end of the clonic phase of the convulsion, when the rabbit was lying in a relaxed state, the E.Co.G. was completely flat; 1–3 minutes after stimulation slow δ-waves of varying voltage appeared. The normal high-frequency E.Co.G. was not usually seen until at least 5 minutes after the shock, and then only intermittently; the frequency was often slightly lower than normal at this stage (4–6 cyc./sec.). In some animals no high frequencies appeared until 8 minutes after stimulation, but in every experiment the normal 6–8 cyc./sec. rhythm was well established between 20 and 60 minutes after stimulation; the record was then indistinguishable from the pre-ictal one of the same animal.

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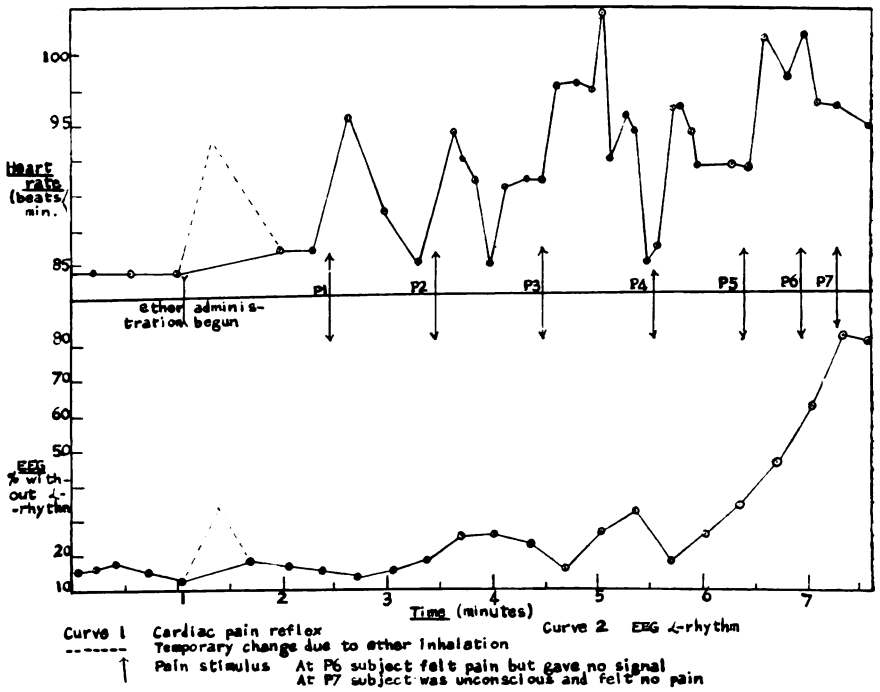


FIG. 3.—Effect of anæsthesia on cardiac pain reflex and E.E.G. in man.

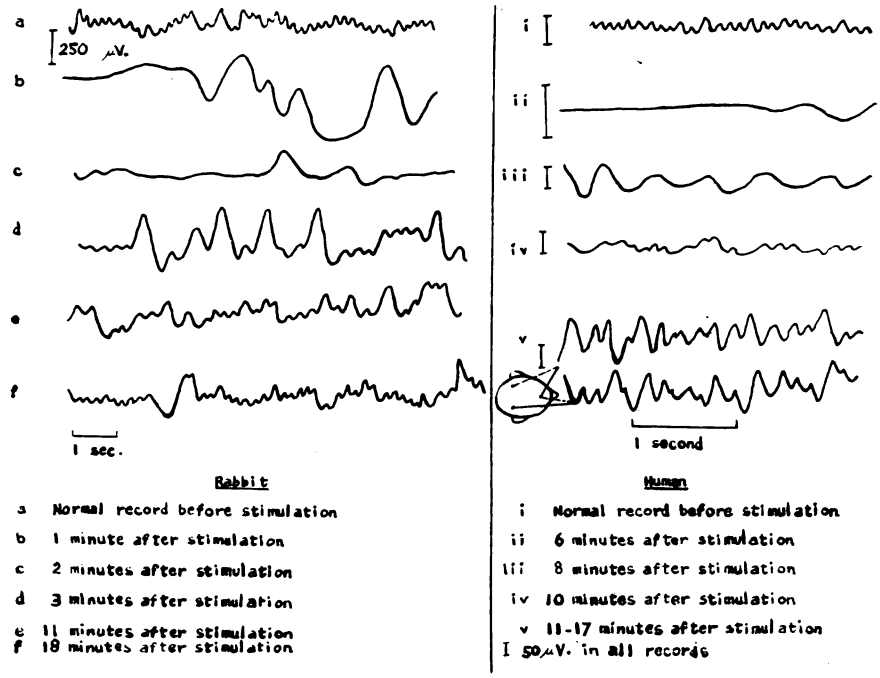


FIG. 4.—Effect of electro-convulsant stimulation on rabbit E.Co.G. and human E.E.G.

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Comparable changes occurred in human E.E.Gs. after electro-convulsant therapy, but the time intervals were longer than in the rabbit E.Co.Gs. The record consisted mainly of δ-rhythm for the first 10 minutes after E.C.T., and the patient appeared quite unconscious during this period; the δ-rhythm was then gradually replaced by bursts of faster frequencies, and the patient opened his eyes and made uncoordinated movements, but did not recognize the people round him. Between 10 and 20 minutes after E.C.T. the E.E.G. often showed long bursts of θ-rhythm (7 cyc./sec.); the phase relations of this rhythm indicated that it had a sub-cortical origin, probably in the diencephalon. α-rhythm reappeared 30–45 minutes after E.C.T. and the patient's responses to questions and commands were normal at this time (Fig. 4).

Discussion.

Experiments showed that the cardiac pain reflex could safely be used as an indicator of consciousness of pain in human and animal subjects, and since it did not involve voluntary muscle, it was valid during states of curarization. The exact regions of the brain involved in this reflex are not known; the afferent impulse travels by the lateral spino-thalamic tract to the ventral part of the lateral thalamic nucleus, and the efferent path is from the cortex to the vaso-motor centre in the medulla. The association area between the afferent and efferent sides is uncertain, but when the reflex is positive, part at least of the thalamus and the cortex must be functional.

After electric shock in the rabbit there is definitely a short period when the c.p.r. is positive whilst the paw reflex is still absent, and a comparable condition has been noted by Hume (1935) in man after electrical accidents. Voluntary muscle apparently cannot function as the final link in a reflex at this stage, and the existence of this condition, when pain can be appreciated but voluntary movement cannot be made, is a factor which should be considered in future work on electrical anaesthesia.

There is abundant evidence that the E.E.G. and the state of consciousness are closely linked (Lowenbach and Lyman, 1940; Martin, 1949; Brazier, 1948; Gibbs, Davis and Lennox, 1935; Swank and Foley, 1948; Adrian, 1947), and Bickford (1950, 1951) has actually devised an apparatus in which the summated cortical potentials operate the plunger of a syringe containing an anesthetic solution, so that any desired level of anaesthesia can be automatically maintained. Faulconer, Pender and Bickford (1949) found that the α-rhythm of man was a good guide to the state of consciousness during the induction and recovery stages of anaesthesia. Lewy and Gammon (1940) have described a 5 cyc./sec. rhythm as the α-rhythm of the rabbit; in the experiments described in this paper the constant rhythm was a 6–8 cyc./sec. one, and although it did not arise from a part of the cortex comparable with that which gives rise to the α-rhythm in man, it was an equally good indicator of the state of consciousness during chemical anaesthesia, and was therefore carefully studied in the E.Co.G. after electrical stimulation.

The E.E.G. of both man and rabbit was flat at the end of the clonic phase following electro-convulsive shock, but after a short period δ-waves appeared; these waves are generally considered to have a sub-cortical origin, and hence their appearance on the cortex indicates that the cortex itself is inactive. Walter (1936) has noticed the widespread appearance of δ-waves simultaneously with loss of consciousness in man, and Lennox *et al.* (1951) associated the appearance of δ-waves in monkey E.E.Gs. with a condition of stupor.

After this stuporose stage the δ-rhythm is interrupted by bursts of faster rhythm, and therefore, presumably, the cortex is becoming active again. The cardiac pain reflex is positive at this stage but there is paralysis of voluntary muscle; it appears that only certain parts of the cortex have recovered their function. Jewsbury (1951) considers that perception of pain *can* be performed by large areas of the cortex, and it can thus occur when recovery from electric stimulation is incomplete.

Finally, normal α-rhythm is re-established indicating that the cortex is fully integrated with sub-cortical structures, and at this stage the subject has regained control of the voluntary muscles. Thus, the results indicate that the cardiac pain reflex is a reliable and convenient method of assessing pain perception, and that it is particularly useful in conditions of curarization when the voluntary muscles are paralysed by electrical or chemical means.

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SUMMARY.

(1) A reflex is described by means of which pain perception in man and animals can be assessed when voluntary musculature is paralysed.

(2) Rabbit E.Co.Gs. and human E.E.Gs. in various stages of anaesthesia and after electro-convulsant shock are described.

(3) The functional activity of the brain responsible for the observed records is discussed.

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