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SCRATCHING MOVEMENTS EVOKED BY DRUGS APPLIED TO THE UPPER CERVICAL CORD

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The following experiments give a description of scratching movements elicited, not reflexly, but by the action of drugs when applied topically to the upper cervical cord. The experiments are the outcome of an incidental observation made in cats anaesthetized with pentobarbitone sodium, in which the dye bromophenol blue was perfused through the cerebral ventricles, and its penetration into the brain tissue was studied (Feldberg & Fleischhauer, 1960). In these experiments perfusion was effected from a cannulated lateral ventricle to the cannulated aqueduct, and as long as the dye did not enter the subarachnoid space no central effects were observed. However, in a few experiments in which the dye leaked out into the subarachnoid space, either along the outside of the aqueductal cannula or because of rupture of the thin roof of the posterior part of the third ventricle, strong myoclonic movements of the hind legs occurred. They were regularly produced when the dye was perfused from the lateral ventricle to the cisterna.

These findings suggested that bromophenol blue had a central excitatory action when present in the subarachnoid space but not when passing through the cerebral ventricles or the aqueduct. When trying to locate the site of action of bromophenol blue by topical application to different parts of the cerebrum, cerebellum, brain stem and spinal cord, it was found that the myoclonic movements could be elicited only from a restricted area of the dorsal surface of the upper cervical cord and that they showed a striking resemblance to those of a normal scratch reflex. Further, similar scratching movements were obtained from the same area with tubocurarine, which is known to produce muscular effects also when perfused from the lateral ventricle to the aqueduct, that is, without passing into the subarachnoid space (Feldberg & Malcolm, 1959).

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METHODS

The experiments were performed on anaesthetized cats. Usually, and if not otherwise stated, anaesthesia was effected by intraperitoneal injection of pentobarbitone sodium (35 mg/kg); additional pentobarbitone was injected during the course of a prolonged experiment. In a few experiments intravenous chloralose (80 mg/kg) was used. The trachea was cannulated and, with the cat lying on its belly, the head was fixed to the ear bars and mouthpiece of a head holder similar to the Horsley Clark stereotaxic instrument. The muscles covering the atlanto-occipital membrane and the epistropheus were dissected away, and the arcs of the atlas and epistropheus were removed, care being taken not to open the venous sinuses on each side. The margin of the supra-occipital bone at the border of the foramen magnum was nibbled away, exposing the lower part of the vermis. The dura was then opened in the mid line and folded back, so as to expose the dorsal surface of the lower part of the medulla oblongata and of the upper cervical cord, for the topical application of either bromophenol blue or tubocurarine solutions.

When the solutions were applied to one side of the cord only, the applicator was a cotton wick threaded through a syringe needle in such a way that about 1 cm of the wick protruded from the tip of the needle, which was kept in a vertical position. The protruding end of the cotton wick was placed on the selected region and a continuous slow flow of solution was maintained by keeping the upper end of the needle filled. When applied to both sides of the cord, a small swab of cotton wool soaked in the solution was placed on the selected region. In order to ensure a good penetration of the topically applied solutions into the tissue of the cord, it was essential that the surface of the cord was not allowed to dry or to become covered by a film of clotted blood.

The sodium salt of bromophenol blue and the tubocurarine were dissolved in artificial c.s.f. The composition of this solution has been described by Merlis (1940). The bromophenol blue was obtained commercially (British Drug Houses) as the acid. It is a powder insoluble in water. The water-soluble sodium salt was prepared by grinding the powder in a mortar with equimolecular amounts of N/10-NaOH; i.e. about 6 ml./400 mg powder, as described previously (Feldberg & Fleischhauer, 1960). The sodium salt has a blue-violet colour.

The tibialis anterior muscles were chosen when it was intended to record the muscular effects from the flexor muscles of the hind legs. With the legs in a flexed position, both tibiae were fixed on a Brown–Schuster myograph stand and the freed tendons of the tibialis muscles were attached to myographs. The contractions were recorded on a smoked drum.

RESULTS

In cats under pentobarbitone sodium anaesthesia strong muscular effects resembling the pattern of the scratch reflex are obtained when a 0·2 or 1 % solution of bromophenol blue or a 0·1 % solution of tubocurarine is applied to the dorsal surface of the spinal cord at the level of C1. In Fig. 1 the shaded area is the region from which this pattern of muscular activity is obtained. When the solutions are applied a little lower than this region, or to the exposed dorsal surface of the lower thoracic cord, no muscular effects are obtained.

When the bromophenol blue or the tubocurarine is applied to one side of the region from which the muscular effects are elicited, the scratching movements occur on that side only. They are sometimes preceded by fasciculation of the muscles in the thigh and in the lower part of the back.

This fasciculation is predominantly ipsilateral and occurs 2–3 min after the topical application. The scratching movements begin a little later in the ipsilateral hind leg with a strong sustained flexion at the hip, and the foot is brought forward along the side of the body. From this position strong myoclonic bursts of movement of the leg are set off by rhythmic alternate flexion and extension at the hip, knee and ankle. There is plantar flexion

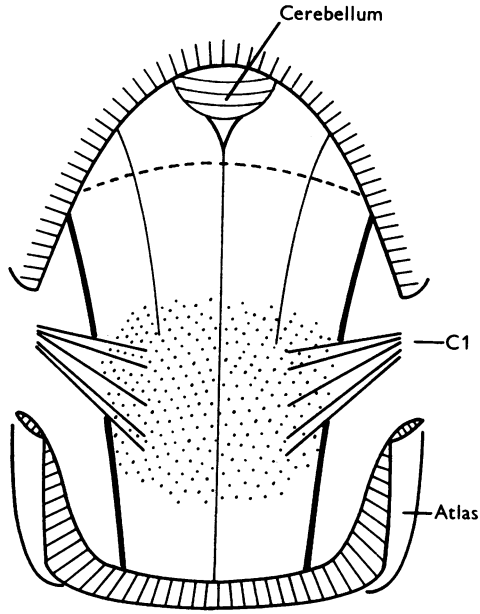

Fig. 1. Diagram of exposed dorsal surface of upper cervical cord of the cat. The stippled area is the region from which scratching movements are obtained with bromophenol blue and tubocurarine. The lower margin of the occipital bone and the arc of the atlas, except its lower rim, have been nibbled away. C1, dorsal roots of first cervical nerve. The interrupted line indicates high transverse section which does not abolish the effect.

of the digits, so that the paw becomes claw-shaped, and the claws are partly extruded. These bursts of scratching movements occur at irregular intervals and are often associated with a steady extension and forward thrust of the ipsilateral foreleg, which is also slowly adducted so that it crosses the mid line. The movement of the foreleg is that which a cat performs when wiping its face. Ipsilateral twitching of the ears and of the facial muscles occurs regularly during these scratching bursts and sometimes also in the intervals. During the scratching movements there is an increase in extensor tone in the contralateral hind leg, which sometimes becomes rigidly extended.

In most experiments the head was fixed in a head holder; thus any head

and body movements which might accompany the scratching movements were masked or prevented. However, in those experiments in which the head was taken out of the holder it became evident that the scratching movements were associated with the postural attitude taken up by a cat when scratching itself behind the ear. The vertebral column was bent with its concavity directed towards the scratching limb, the head was turned to the same side and then rotated so that the claws of the scratching foot touched the skin behind the ear.

When the bromophenol blue or the tubocurarine is applied to both sides of the region from which the muscular effects are elicited, the scratching movements occur in both hind legs, but at different times. They start in one hind limb and when they come to an end they may be immediately followed by similar scratching movements in the opposite hind limb, and so the scratching movements continue alternating from one hind limb to the other, or there may be periods of rest in both hind limbs between these alternating scratching movements. When the scratching movements alternate quickly from one hind limb to the other, and the head is fixed in a head holder, the slow steady extension and adduction of the corresponding forelegs does not keep pace with the quick alternation, with the result that the forelegs cross. When this quick alternation occurs with the head taken out of the head holder, the bending of the spine and turning and rotation of the head also occurs alternately from one side to the other. Apart from these movements there is a general increase in tone of the body musculature instead of the usual relaxation of muscle tone present in pentobarbitone sodium anaesthesia.

In two cats which were decerebrated at mid-collicular level in pentobarbitone sodium anaesthesia, the topical application of bromophenol blue to the region of the spinal cord shown by the stippled area in Fig. 1 produced the same muscular effects as in the non-decerebrate cats.

Penetration of bromophenol blue into the tissue of the cervical cord

In several experiments, in which the topical application of 0·2 % bromophenol blue with a cotton swab to both sides of the dorsal surface of the cervical spinal cord at the level of C1 had led to the typical bursts of scratching movements, cross-sections of the cord were made at this level at the end of the experiment and examined with the naked eye for penetration of the dye into the tissue of the cervical cord. It was found that within half an hour the dye had penetrated about 1–2 mm into the nervous tissue; with longer periods of topical application there was little increase in the depth of penetration but the staining became more intense. Usually the zona gelatinosa Rolandi stood out within the stained area as a more intensely stained region, as illustrated in the diagram of Fig. 2.

Myographic recordings from the anterior tibialis muscles of cats in pentobarbitone anaesthesia

Bromophenol blue. When the dye is applied to the region of the cervical cord shown by the shaded area in Fig. 1, it causes contractions of the tibialis muscles, but not when it is applied to lower regions of the cervical, or to the dorsal surface of the thoracic cord. The concentration of dye used was usually 0·2 % but sometimes 1 %.

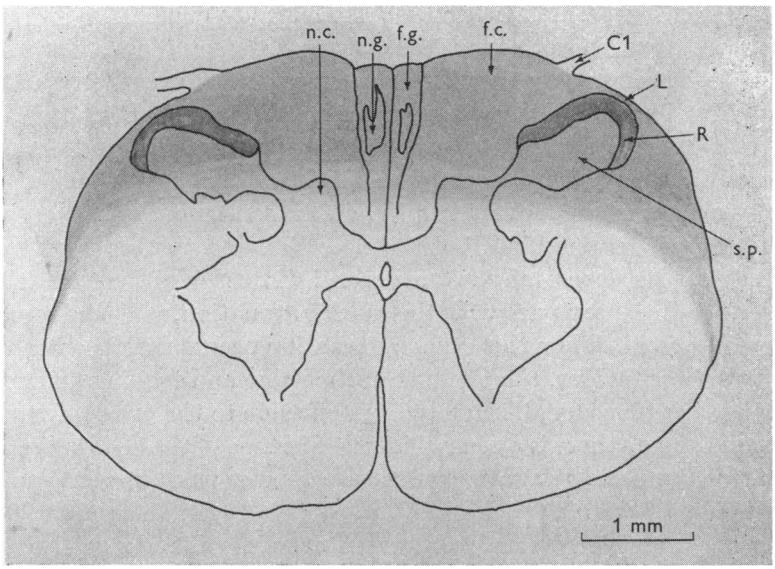

Fig. 2. Cross-section of cat's spinal cord at level of C1. Penetration of bromophenol blue 30 min after topical application to the dorsal surface shown by darkened area. Zona gelatinosa Rolandi (R) stands out, being more intensely stained. n.c. and f.c., nucleus and fasciculus cuneatus; n.g. and f.g., nucleus and fasciculus gracilis; C1, entrance of first cervical dorsal root; L, area of Lissauer; s.p., stratum spongiosum internum. Terminology from Winkler & Potter (1914).

When the dye is applied to one side of the region shown by the shaded area of Fig. 1, the effect occurs in the ipsilateral tibialis muscle only; it usually begins after a latency of 3–10 min with a few irregular and comparatively weak contractions followed by a burst of strong rhythmic contractions. Similar bursts recur at irregular intervals and usually follow a typical pattern. They begin with a sustained contraction, a strong tension is built up step-wise, then it suddenly gives way, relaxation becomes either complete or partial and the muscle is thrown into vigorous rhythmic activity. The duration of a burst as well as the strength and frequency of

its rhythmic contractions vary in different experiments and also in the course of the same experiment.

Figure 3 illustrates two typical bursts. The upper record shows a burst in which there is complete relaxation of the initial sustained contraction and again after each subsequent contraction of the rhythmic activity. This was the more usual occurrence. The record further illustrates the irregular

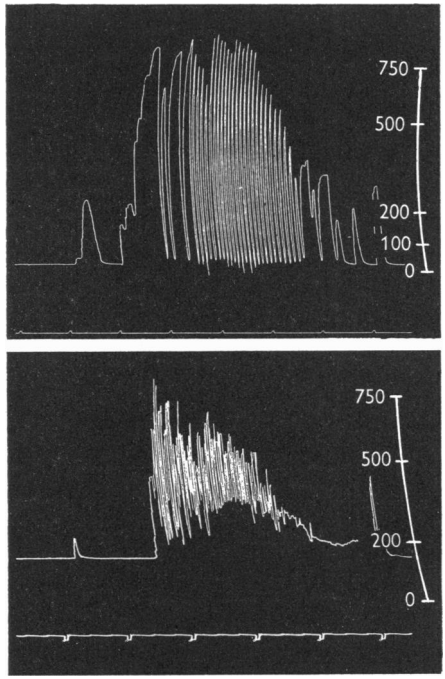

Fig. 3. Records from anterior tibialis muscle of two cats under pentobarbitone sodium anaesthesia. Two types of bursts of scratching movements obtained on topical application of 0·2% bromophenol blue to the dorsal surface of the upper cervical cord. Upper record: scratching movements at a frequency of 1·3/sec after initial strong contraction; complete relaxation between beats. Lower record: frequency of the scratching movements 3·3/sec; incomplete relaxation between beats. On the right, tension in grams. Time marker, 10 sec.

reduced and more sustained contractions at the end of the burst. The lower record is from a different experiment. The initial sustained contraction of the burst relaxes slightly only before the onset of the rhythmic activity and relaxation between successive rhythmic beats is also incomplete. The frequency of beats is about 1·3/sec in the burst of the upper, and about 3·3/sec in that of the lower record. In both records the initial strong sustained contraction of the burst is preceded by a smaller sustained contraction. Sometimes several such small sustained contractions occur a few seconds before the onset of the actual burst.

Before each burst the tibialis muscle is either relaxed or undergoes irregular contractions, which are weaker and occur at lower frequencies than the bursts, so that these stand out clearly. Sometimes, however, bursts are no longer distinguishable from the almost continuous activity which varies in intensity from time to time. In the same experiment the pattern of activity may change from discrete bursts separated by periods of rest to an almost continuous activity.

During the bursts of the anterior tibialis muscle other muscles of the same limb undergo similar rhythmic contractions, but as long as the dye does not diffuse across the mid line no contractions occur in the opposite hind limb and its tibialis muscle remains relaxed.

In two experiments in which the topical application of bromophenol blue had produced almost continuous activity of the tibialis muscle this activity ceased as a spontaneous emptying of the bladder occurred, and began again after micturition.

When the bromophenol blue is applied to both sides of the spinal cord, at the region shown by the shaded area in Fig. 1, the tibialis muscles become active in both limbs but they contract alternately. The onset of a burst in one tibialis muscle causes cessation of contraction in the other and when this muscle again begins to contract, the activity in the former ceases. This alternation, which is illustrated in Fig. 4, shows certain variations. A burst of activity may start in one tibialis muscle immediately or a short time after the activity in the other has come to an end. Or, when the bursts are of short duration and occur infrequently, one, two or three may occur in the same tibialis muscle during a relatively long period of rest in the other. At other times a burst in one tibialis muscle may start during the final weak contractions of a subsiding burst in the other; or again a burst may start in one whilst the other relaxes from a strong sustained contraction, which may have been the initial phase of a burst cut short by the onset of the burst in the muscle of the other side. This is seen in Fig. 4. The onset of the last burst in the left tibialis muscle coincides with the relaxation from a strong sustained contraction of the right muscle. There is not only an alternation of activity in both tibialis muscles but the pattern of activity may be different too; discrete infrequent bursts may be evoked in one and long periods of almost continuous activity in the other.

The fact that the onset of activity in one tibialis muscle is the cause of cessation of activity in the other is sometimes strikingly illustrated in experiments in which the dye is applied first to one and then to the other side. When the first application has produced almost continuous activity in the one muscle and the dye is then applied to the other side, this activity ceases abruptly with the onset of activity in the other muscle.

When the dye is removed and the surface of the cervical cord is frequently rinsed with artificial c.s.f., the muscular activity in the tibialis muscle subsides and ceases within 40–60 min, but on re-application of the dye it returns.

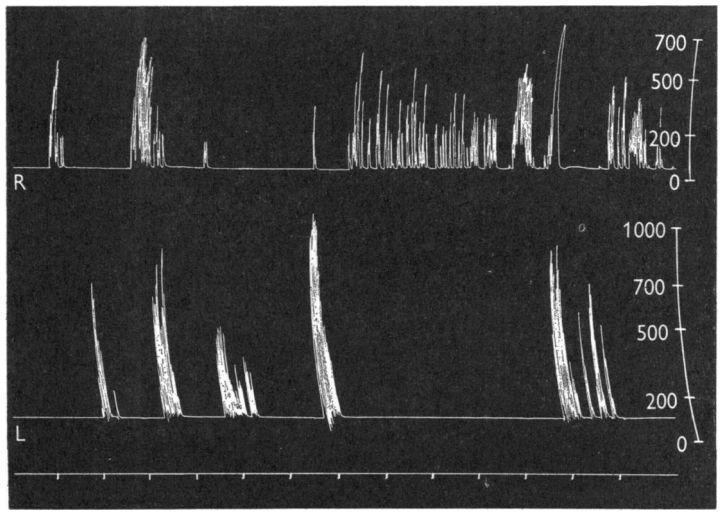

Fig. 4. Record of alternating activity in right (R) and left (L) anterior tibialis muscle of a cat under pentobarbitone sodium anaesthesia a few minutes after topical application of 0·2 % bromophenol blue to both sides of the exposed dorsal surface of the upper cervical cord. On the right, tension in grams. Time marker, 10 sec.

Tubocurarine. The topical application of tubocurarine, in a 0·1 % solution, to the dorsal surface of the spinal cord has the same effect as bromophenol blue. Applied to the region shown by the shaded area in Fig. 1 it causes contractions of the tibialis muscles, but applied at a lower level of the cervical cord it is ineffective. Applied to one side the effect occurs on the ipsilateral tibialis muscle, applied to both sides both tibialis muscles become alternately active. Between the application of the tubocurarine and the onset of contractions there is a latency of 5–15 min, which is on the average a little longer than after bromophenol blue, and on removal of the tubocurarine the activity subsides more quickly than after removal of the bromophenol blue. The pattern of activity of the tibialis muscle is the same as after bromophenol blue. There are the discrete characteristic bursts of rhythmic contractions, but the activity may change to an almost continuous one. Some of these results are illustrated in Figs. 5 and 6.

Figure 5 shows the beginning of muscular activity in the left anterior tibialis muscle a few minutes after the topical application of tubocurarine

to the same side of the cervical cord. A few short-lasting contractions are followed by discrete bursts, the last one being taken with a quicker speed of the drum to show the frequency of the rhythmic contractions, which is about 2/sec.

Figure 6 shows that after rinsing the surface of the spinal cord with artificial c.s.f. following removal of the tubocurarine, the activity diminished relatively quickly. The tubocurarine had been applied to the right side of the cord for 15 min. Sections *A*, *B* and *C* begin 4, 11 and 14 min,

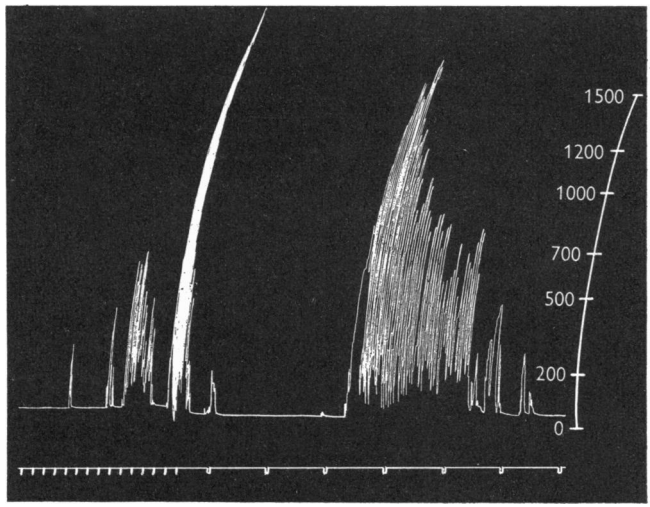

Fig. 5. Record of left anterior tibialis muscle of a cat under pentobarbitone sodium anaesthesia a few minutes after topical application of 0·1 % tubocurarine to the left side of the exposed dorsal surface of the upper cervical cord. A few initial irregular contractions followed by bursts of scratching movements occur, the last one being recorded on a faster moving drum. Frequency of beats: 2/sec. On the right, tension in grams. Time marker, 10 sec.

respectively, after its removal. At 4 min the activity of the right tibialis muscle had not perceptibly diminished; the contractions were as strong as during the time of tubocurarine application. At 11 min the individual beats in each burst have become much weaker and at 14 min there is a further attenuation. At the beginning of section *C* 0·2 % bromophenol blue has been applied to the left side of the spinal cord; 6 min later strong contractions begin in the left tibialis muscle and with the onset of this activity all contractions of the right muscle cease.

In some experiments records from both tibialis muscles were taken after decerebration in pentobarbitone sodium anaesthesia and the tubocurarine was first applied to the left side and later to both sides of the cervical cord. In the experiment of Figs. 7 and 8, decerebration was performed 2 hr

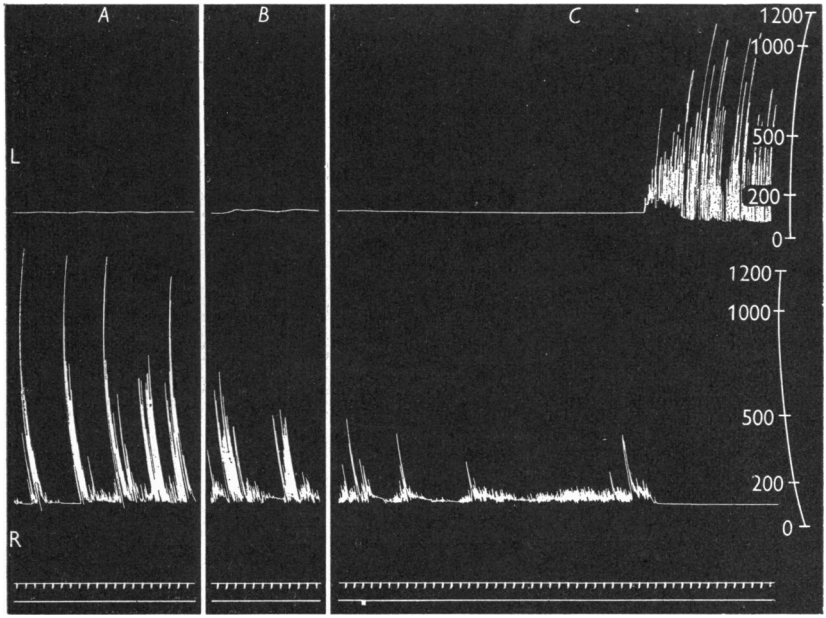

Fig. 6. Records of left (L) and right (R) anterior tibialis muscles of a cat under pentobarbitone sodium anaesthesia. Record *A* begins 4, record *B* 11, and record *C* 14 min after removal of tubocurarine (0·1 %), which had been applied for 15 min to the right side of the exposed dorsal surface of the upper cervical cord. The records show the attenuation of activity in the right muscle which comes to an abrupt end when, on application of 0·2 % bromophenol blue (at the signal on bottom line) to the left side of the exposed dorsal surface of the upper cervical cord, activity begins in the left muscle. On the right, tension in grams. Time marker, 10 sec.

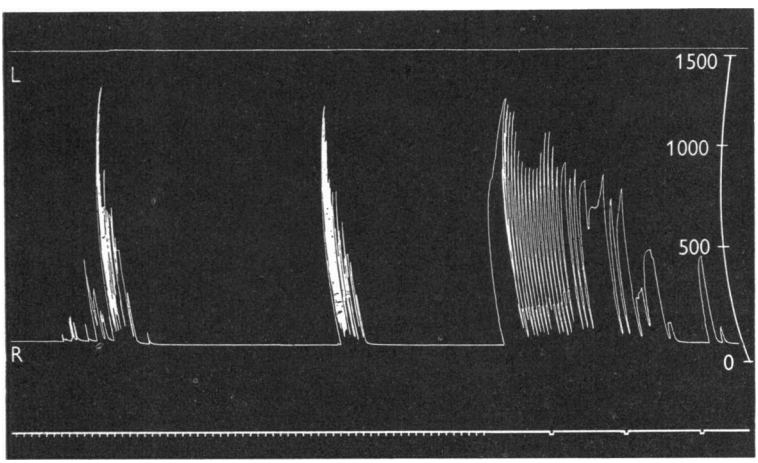

Fig. 7. Records of left (L) and right (R) anterior tibialis muscles of a cat decerebrated under pentobarbitone sodium anaesthesia. Tubocurarine (0·1 %) applied to the right side of the exposed dorsal surface of the upper cervical cord. The record shows the beginning of activity in the right muscle. On the right, tension in grams. Time marker, 10 sec.

after the pentobarbitone sodium injection; Fig. 7 shows the effect of the unilateral application of tubocurarine. After a latency of 14 min, activity begins in the right muscle with a few irregular contractions followed by three discrete bursts of strong rhythmic beats. As the onset of each burst

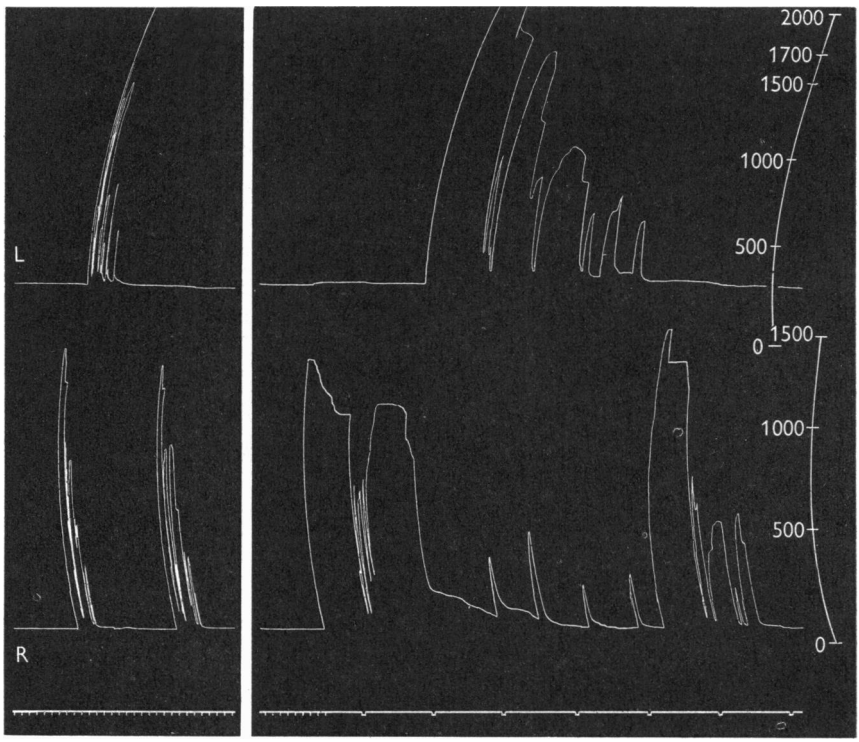

Fig. 8. Records of left (L) and right (R) anterior tibialis muscles of a cat decerebrated whilst under pentobarbitone sodium anaesthesia. Continuation of Fig. 7, 2 hr later. Tubocurarine (0·1 %) applied to both sides of the exposed dorsal surface of the upper cervical cord. On the right, tension in grams. Time marker, 10 sec.

was preceded by a few weak myoclonic movements of the paws it was easy to increase the speed of the drum just before the onset of the third burst and thus to show its individual beats: they occurred at a frequency of about 2/sec. The left tibialis muscle remained inactive throughout the unilateral application of the tubocurarine. When later it was applied to both sides, discrete bursts occurred in both tibialis muscles, but the periods of activity alternated. In this experiment it was found that at this late stage, about 3 hr after the decerebration, the bursts consisted of fewer but longer-sustained contractions. The alternation and this change in the character of the bursts is illustrated in Fig. 8.

In one experiment a transverse section was made with a thermocautery through the medulla oblongata just below the obex. This did not abolish the muscular contractions but they became attenuated and occurred less frequently.

Chloralose anaesthesia

In experiments carried out for another purpose together with A. B. Cairnie and J. L. Malcolm, it was found that the scratching movements, elicited in cats under pentobarbitone anaesthesia by the topical application of bromophenol blue or tubocurarine to the upper cervical cord, did not occur in cats under chloralose anaesthesia, although in this condition tubocurarine still produced muscular effects by acting on more rostral

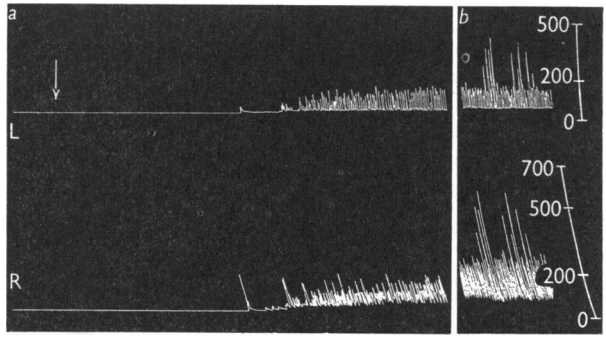

Fig. 9. Records of left (L) and right (R) anterior tibialis muscles of a cat under chloralose anaesthesia. Topical application of 0·1 % tubocurarine to the exposed dorsal surface of the upper cervical cord had produced no muscular activity. At the arrow (↓) 200 μg tubocurarine injected into the cannulated left lateral ventricle. On the right, tension in grams. Time marker, 10 sec.

parts of the neuraxis (Feldberg & Malcolm, 1959). Such an experiment with chloralose anaesthesia is illustrated in Fig. 9. First, tubocurarine 1/1000 was applied to both sides of the exposed dorsal surface of the cervical cord at the region of C 1 for 30 min; no contractions of the anterior tibialis muscle or any other muscular action ensued. Then, at the arrow in Fig. 9, 200 μg of tubocurarine was injected through a Collison cannula implanted into the left lateral ventricle. About 5 min later there occurred generalized fasciculation, tremor-like activity and frequent small jerk-like contractions of the shoulders and thorax, which later led to small jerks of the whole animal. There was no indication, however, of either scratching movements or of alternating activity between the right and left hind legs. Figure 9 shows the records taken from both tibialis anterior muscles. At first (at *a*) tremor-like activity only was recorded; later, at *b*, this activity was interspaced by somewhat stronger contractions which reflected the small jerks of the whole animal in these muscles.

The finding that under chloralose anaesthesia no scratching movements are produced by topical application of the tubocurarine to the upper cervical cord cannot be explained by an inability of the tubocurarine to penetrate into the tissue of the spinal cord in this condition, as is evident from the following result. When the scratching movements have been produced under pentobarbitone anaesthesia and the topical application of the drug is continued whilst chloralose 70 mg/kg is injected intravenously, they immediately become attenuated and cease within a few minutes.

DISCUSSION

The finding that in cats under pentobarbitone sodium anaesthesia topical application of either bromophenol blue or tubocurarine to the dorsal surface of the exposed upper cervical cord produces a pattern of muscular activity resembling that seen in the scratch reflex, and that the application to one side of the cord produces the scratching movements in the hind leg on the ipsilateral side, suggests a selective activation of the long descending propriospinal neurones in the lateral column of the spinal cord, which on stimulation of the skin mediate the scratching movements of the hind legs, as was shown by Sherrington & Laslett (1903) in their classical experiments of successive degeneration.

An indirect activation of these neurones by an excitatory action of the substances on the cells of the nuclei gracilis and cuneatus can be excluded, because the scratching movements were also obtained after decerebration whereas the fibres from these nuclei are known to be ascending afferent ones and to relay almost entirely in the contralateral thalamus (Matzke, 1951; Bowsher, 1958). Therefore the substances must act at the synapses where the sensory fibres from the skin impinge either directly or through internuncials on the large descending propriospinal neurones, and the action may well be an excitation or depolarization of the cell bodies of these neurones.

The fact that the topical application of the substances to a restricted area of the cervical cord imitates the whole pattern of movements associated with the scratch reflex, i.e. not only the scratching movements of the hind leg but also the postural changes of the body which are an accompaniment of this reflex and such movements of the foreleg as a cat performs when wiping its face, would be difficult to understand if the substances were to act indiscriminately on all synapses present in this region and reached by the bromophenol blue and tubocurarine when penetrating through the superficial layers of the cord. The action must therefore be a highly selective one confined to those neurones in the upper cervical cord which are activated in the scratch reflex by the afferent impulses from the skin; or, in other words, the action must be selectively on those

neuronal structures which form the 'reflex centre' for the scratch reflex in this region.

Pentobarbitone sodium is generally considered to have a more profound central depressant action than chloralose, which has some of the properties of a convulsant besides those of an anaesthetic (Adrian & Moruzzi, 1939). Yet in chloralose anaesthesia neither bromophenol blue nor tubocurarine elicited the scratching movements. This finding could indicate that chloralose is more depressant on the spinal cord and pentobarbitone on the more rostral parts of the neuraxis. An alternative explanation would be that chloralose has a specific depressant action on the neuronal system that is activated when the topical application of bromophenol blue or tubocurarine elicits the scratching movements. For instance, if no internuncial neurones, or only a few, were taking part in this activation, the results might suggest that the depressant action of pentobarbitone is more on internuncial activity, that of chloralose more on neurones or their cell bodies which form long pathways in the spinal cord, such as the long descending propriospinal fibres.

From the finding that the scratching movements occur in pentobarbitone but not in chloralose anaesthesia, it does not necessarily follow that pentobarbitone has no depressant effect on this phenomenon. It would be sufficient to assume that its depressant action is weaker than that of chloralose. Recent experiments (F. R. Domer & W. Feldberg, unpublished) carried out to investigate this problem have in fact shown that pentobarbitone, too, exerts a depressant effect on the scratching movements obtained by the topical application of tubocurarine. These experiments made it also possible to explain why, in one of the present experiments, the bursts of activity obtained with tubocurarine in a cat decerebrated in pentobarbitone sodium anaesthesia consisted of more sustained muscular contractions. It was found that pentobarbitone could convert such sustained contractions into typical bursts of fast rhythmic activity. It is therefore reasonable to conclude that in the specific experiment described in this paper the effect of pentobarbitone had worn off, particularly since the sustained contractions were obtained 3 hr after the decerebration, which again was performed 2 hr after the pentobarbitone sodium injection. This experiment thus revealed the type of muscular activity which may occur on the topical application of tubocurarine in the unanaesthetized decerebrate cat.

Although both bromophenol blue and tubocurarine elicit the scratching movements when applied to the upper cervical cord, they differ pharmacologically in their peripheral as well as in their central effects. Bromophenol blue lacks not only the neuromuscular blocking action (K. Fleischhauer, unpublished experiments), but also the other central motor effects which

tubocurarine exerts on more rostral parts of the neuraxis. In fact, as was stated in the introduction, the starting point for the present experiments was the observation that bromophenol blue, unlike tubocurarine, did not produce muscular contractions when perfused through the cerebral ventricles, but did so when it reached the subarachnoid space. These observations were made in cats anaesthetized with pentobarbitone sodium. It is naturally not certain whether the same condition pertains in unanaesthetized cats. In these the injection of bromophenol blue into the cerebral ventricle produces strong muscular effects of a convulsive type (unpublished experiments). It would be interesting to know whether this effect is entirely the result of the dye reaching the subarachnoid space, or if there is in addition some contribution due to an action on the grey matter surrounding the aqueduct and the cerebral ventricles. If the effect were entirely one produced on the spinal cord when the dye reaches the subarachnoid space, it would mean that, at least in the cat, a convulsive type of activity can result from an action of drugs activating descending pathways in the upper cervical cord, and that exaggerated scratching movements may form the basis of a convulsive activity. These considerations apply also to a number of other drugs which on injection into the cisterna magna produce convulsions.

Finally, it must be pointed out that the excitatory action of tubocurarine on the upper cervical cord which results in the scratching movements is not the cause of the striking changes in electrical activity of the brain which occur when this substance is injected into the cerebral ventricles and which resemble so closely the seizure discharges of epilepsy. This is evident from the fact that the electrical changes occur also in cats that are anaesthetized with chloralose (Feldberg, Malcolm & Smith, 1957), although in this condition tubocurarine does not elicit the scratching movements. Further A. B. Cairnie and J. L. Malcolm (personal communication) obtained the electrical changes also when tubocurarine was perfused from the lateral cerebral ventricle to the aqueduct and did not reach the subarachnoid space. On the other hand, the electrical changes could not be reproduced by the topical application of tubocurarine to the upper cervical cord, as was shown in preliminary experiments together with Cairnie and Malcolm.

SUMMARY

1. There is a restricted region of the upper cervical spinal cord, at the level of C 1, from which it is possible to elicit regularly, in cats anaesthetized with pentobarbitone sodium, scratching movements of the hind limbs by topical application to the dorsal surface of either 0·2 % bromophenol blue or of 0·1 % tubocurarine. The scratching movements are associated with

postural changes, the attitude being that of a cat scratching itself behind the ear. Further, the forelegs perform movements which resemble those which a cat performs when wiping its face.

2. The scratching movements of the hind legs were recorded myographically from the anterior tibialis muscles.

3. The scratching movements occurred usually in bursts. When the topical application of bromophenol blue or of tubocurarine was to one side of the cord they occurred, with the associated movements of the foreleg, on the ipsilateral side only. When the topical application was to both sides, bursts occurred alternately on either side.

4. Decerebration at mid-collicular level did not abolish the motor effects obtained on topical application of either bromophenol blue or tubocurarine to the dorsal surface of the upper cervical cord.

5. In chloralose anaesthesia motor effects could not be elicited on topical application of either bromophenol blue or tubocurarine to the dorsal surface of the upper cervical cord.

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