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EFFECTS OF MEPHENESIN AND CHLORPROMAZINE ON MOTOR NERVE DISCHARGES IN THE RABBIT

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Although many hypnotic, sedative and tranquillizing drugs are to some extent centrally acting muscle relaxants, mephenesin is perhaps the only drug that has this effect as a primary action. It is generally believed to achieve this by blocking transmission at spinal interneurones, since it blocks polysynaptic but not monosynaptic reflexes. Chlorpromazine has also been found to produce muscular relaxation in both experimental and clinical tetanus although its mechanism of action probably differs from that of mephenesin (Webster, 1961).

Muscle tone depends not only on the discharge of α-motoneurones to the muscle extrafusal fibres, but also on the reflex activation of this pathway through monosynaptic excitation of the motoneurone by impulses from the muscle spindles (also called intrafusal fibres), which are propioceptive receptors within the muscle itself. The muscle spindles are in turn activated by impulses in smaller (γ) motor nerves and their state of excitability, and consequently the input that they send into the cord, depends on the degree of γ-innervation and the level of activity within the extrapyramidal system of which it forms part.

The effect on these two motor systems of mephenesin and chlorpromazine, in doses known to produce equivalent muscular relaxation (Webster, 1961), has been studied using discharges from α- and γ-motoneurones, recorded in ventral root or motor nerve filaments; and spindle discharges, recorded in dorsal root filaments of the decerebrate rabbit.

METHODS

All experiments were performed on decerebrate rabbits. Surgical anaesthesia was induced with thiopentone sodium (25 mg/kg), administered into a marginal ear vein, and maintained with ether. The trachea was cannulated, both carotid arteries were tied and a polyethylene cannula was inserted into the right femoral vein for drug injections.

Preparations

Ventral root. Clamps were inserted into the lower part of each femur and the extremity of each tibia. The animal was then rigidly fixed to the myograph stand, additional clamps being placed on the spinous process of the 4th lumbar vertebra and across the two ischial tuberosities of the pelvic girdle. The head was held firmly in a clamp and the fore-limbs tied securely. Laminectomy was performed from L5/6 to S3 and the sural nerve was exposed for stimulation.

Dorsal root. The animal was fixed as above but the left hind-limb was extensively denervated. The femoral and obturator nerves were first cut and then, through an incision in the left popliteal fossa, all branches of the sciatic and popliteal nerves were cut, apart from those to plantaris and medial gastro-

cnemius muscles. The hamstrings and all nerves to the thigh and tail muscles were cut in the thigh just above the acetabulum of the pelvis. The tendons to plantaris and medial gastrocnemius muscles were exposed and prepared for tension recording.

Motor nerve preparations. For records taken directly from the nerve to medial gastrocnemius the animal was placed on its side and the left hind-limb was fixed in a horizontal plane parallel to the myograph stand by two clamps in the femur and one in the tibia.

At these stages in the above preparations the animals were decerebrated at the intercollicular level, the soft cortical tissue being removed by suction and the blood vessels occluded with a small bulldog clip. In the ventral and dorsal root preparation the dura mater was opened and the appropriate spinal roots were drawn up on to electrodes and split down until a single unit was obtained. In the motor nerve preparation a small filament of the medial gastrocnemius was split down. By the time single units had been obtained and identified the effect of the ether had worn off.

Electrical recordings

All discharges were recorded from one side of bipolar platinum electrodes with the other side either earthed or balanced with an inactive (crushed) filament. Potentials were amplified by a balanced AC-amplifier from a cathode follower input and displayed on a Cossor 1049 oscilloscope. A frequency integrating circuit was used to obtain a direct meter reading of the discharge frequency and to give a DC-potential proportional to frequency for display on an Ediswan pen recorder (Fig. 8). This was used to record both the initial peak and following adapted discharge from muscle spindles. Tension changes were recorded with a Grass strain gauge transducer.

Identification of units

α- and γ-motor fibres were distinguished by characteristic differences in the size and pattern of discharge. α-Impulses are invariably larger and do not usually fire tonically (Fig. 1); when they do so the frequency is

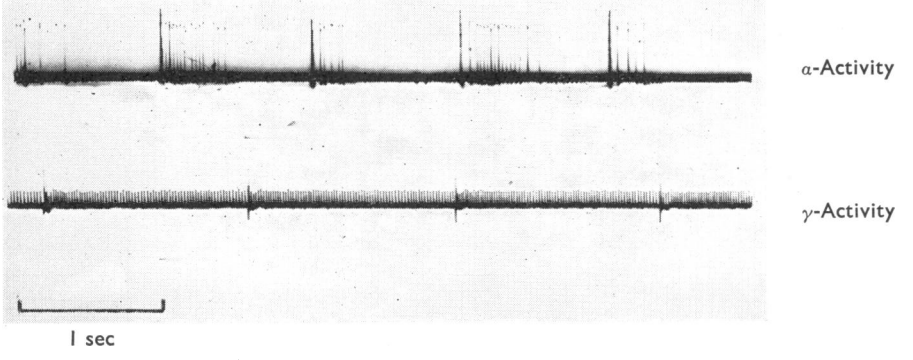

Fig. 1. α- and γ-motor nerve activity recorded from a ventral root filament of a decerebrate rabbit. Single shocks (2 V, 200 μsec) applied to the sural nerve at 1 shock/sec caused phasic firing of the α-unit and increased the discharge of the γ-unit.

below that of most γ-fibres and they are not as responsive to afferent stimuli. γ-Fibres generally fire tonically, are smaller in size and more responsive to stimuli. No attempt was made to measure the conduction velocities of fibres in the ventral roots. Spindles were identified by the pause in discharge during muscle contraction; and the conduction velocity of the afferent fibres was determined. To vary the spindle discharge by varying muscle length, the muscle tendon was connected to a spring balance which was manually pulled to balance readings of 200, 400, 600 and 800 g. The muscle was held at each weight (tension) long enough for the spindle to adapt and further tension was then applied, the weights being cumulative. This procedure was adopted in preference to altering muscle length, since it is easier to arrange and appears to be justified by the reasonable reproducibility of the results.

General

Animals were warmed by indirectly heating the myograph stand from below with two DC electric-fire elements (1 kW) operated through a rheostat. Additional heating was provided by an overhead infra-red lamp. All recording and stimulating electrodes were well covered with paraffin oil (B.P.) equilibrated with distilled water at 37° C. All doses of chlorpromazine are given in terms of the hydrochloride.

RESULTS

α- and γ-motor nerve discharges

Discharges were recorded from ventral root and motor nerve filaments of the decerebrate rabbit. The effects of mephenesin and chlorpromazine, in doses that were known to produce a similar reduction of the electromyogram of conscious rabbits (Webster, 1961), were studied on a number of spontaneously firing α- and γ-motor nerves as well as on the discharge evoked by stimulation of the sensory sural nerve. Generally both drugs reduced or abolished tonic α-activity and depressed or abolished reflex activation of the α-motoneurone, although mephenesin was slightly more effective in this respect than chlorpromazine. γ-Neurones were relatively resistant to mephenesin in doses that blocked α-activity (Fig. 2) but were readily depressed by chlorpromazine. In most experiments it

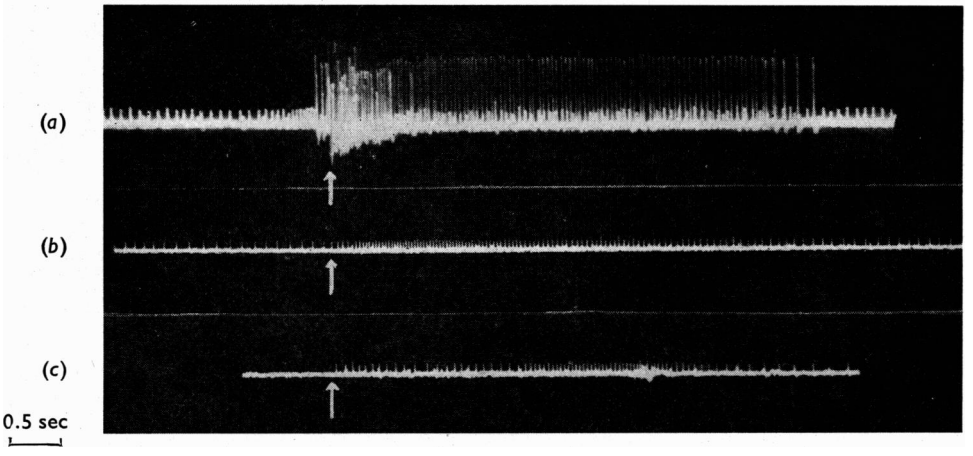

Fig. 2. Mixed α- and γ-discharges in a ventral root filament of decerebrate rabbit. In (*a*) pinching the fore-paw (at arrow) produced a burst of α-firing superimposed on a tonic γ-discharge. After mephenesin, 20 mg/kg (*b*), the tonic γ-discharge was reduced but the same stimulus (at arrow) caused a transient increase. Chlorpromazine (0.25 mg/kg) abolished the tonic γ-discharge (*c*) and further reduced the response to the stimulus (at arrow).

was possible to study the effect of both drugs on single unit discharges (Fig. 3) and to record changes in discharge frequency. The effect of both drugs on fifteen γ-units is shown in Table 1 as well as the effect on some α-units. Mephenesin was always given first since it is short-acting, and when its effect had worn off and the previous control discharge level had returned the effect of chlorpromazine was investigated. Mephenesin (20 mg/kg) reduced the average γ-discharge from 41 to 31 impulses/sec, but chlorpromazine (0.25 to 0.5 mg/kg) reduced it from 39 to 7 impulses/sec. Thus in doses that had previously been found to produce a similar reduction in muscle tone (Webster, 1961) chlorpromazine had a greater depressant effect on γ-activity than had mephenesin.

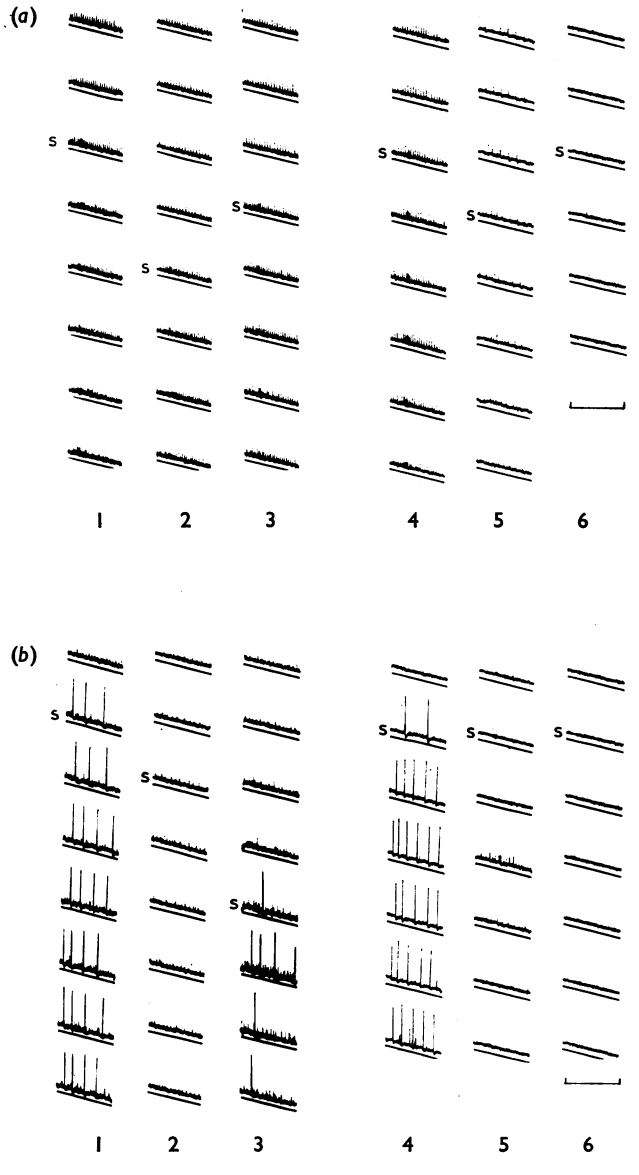

Fig. 3. Some drug effects on single γ- (*a*) and α- (*b*) unit discharges from a ventral root of a decerebrate rabbit. Stimuli (0.5 shocks/sec) were applied to the ipselateral sural nerve at S and in subsequent sweeps in any one series. In both sections (*a*) and (*b*) the series 1, 2 and 3 show activity before and at 1 and 5 min after mephenesin (20 mg/kg) respectively; whilst 4, 5 and 6 show activity before and at 6 and 10 min after chlorpromazine (0.5 mg/kg). Note that although chlorpromazine abolished both α- and γ-activity it became fully effective only after 10 min by which time the effect due to mephenesin was wearing off. Chlorpromazine also produced spontaneous bursts of activity (*b*, 5). Time calibrations, 0.5 sec.

TABLE 1

EFFECT OF MEPHENESIN AND CHLORPROMAZINE ON α- AND γ-MOTOR NERVE ACTIVITY OF DECEREBRATE RABBITS

Records were taken either from ventral root (V.R.) or motor nerve (M.N.) filaments. The control discharge frequency for each γ-fibre is given on the left-hand side of the appropriate column and the discharge at 1 to 2 min after mephenesin or 4 to 5 min after chlorpromazine on the right-hand side. Frequencies are not given for α-fibres as the discharge was generally neither regular nor well maintained. α-Activity was not recorded in all experiments. Two γ-fibres were studied in experiment 9. In all experiments mephenesin was given first, since it is short acting, and when its effect had worn off chlorpromazine was injected

		Mephenesin			Chlorpromazine		
			Effect on			Effect on	
Expt. No.	Preparation	Dose (mg/kg)	α-Fibre	γ-Fibre (imps/sec)	Dose (mg/kg)	α-Fibre	γ-Fibre (imps/sec)
1	M.N.	20		55–40	0·25		58– 0
2	V.R.	15		41–40	0·25		45– 0
3	M.N.	20	Abolished	60–35	0·5	Abolished	45–15
4	V.R.	20	Abolished	40–25	0·25	Reduced	35–22
5	V.R.	20	Abolished	32–29	0·5	Abolished	31–15
6	V.R.	20	Abolished	48–38	0·5	Abolished	46–14
7	V.R.	20	Abolished		0·5	Abolished	
8	V.R.	20		12– 9	0·25		12– 0
9	V.R.	20	Abolished	48–32	0·5	Abolished	48– 0
		20		42–36	0·5		42–12
10	V.R.	20		32–29	0·5		32– 0
11	V.R.	20	Abolished	78–50	0·25	Reduced	75– 0
12	V.R.	20		11– 6	0·25		11– 0
13	M.N.	20		46–40	0·25		38–26
14	V.R.	20		19–12	0·5		18– 0
15	M.N.	20		50–40	0·25		48– 0
			Means	41–31			39– 7

There is rarely a great deal of α-activity in a normal decerebrate rabbit unless considerable rigidity is present. Increased α-activity can be achieved if a small dose of tetanus toxin is injected into one gastrocnemius muscle, when a distinct local tetanus develops confined to one limb and its associated motoneurones. Fig. 4 shows two tracings taken from ventral root filaments of both the affected and normal sides of a rabbit with local tetanus. These records show the greater level of α-activity on the tetanus side, the relatively specific effect of mephenesin on α-motoneurones and the potent depressant effect of chlorpromazine on γ-activity.

Chlorpromazine often produced some stimulation both in normal and tetanus animals before its depressant effect became apparent. A spontaneous burst of activity (probably γ) is noticeable in Fig. 3, whilst, in Fig. 5, a clear acceleration of a tonic α-discharge can be seen. This tracing also shows the rapid onset of action of mephenesin compared with that of chlorpromazine.

Experiments were performed to see if the chlorpromazine depression of γ-activity could be reversed by strychnine. It was found in a number of instances that a γ-discharge, which had been abolished by chlorpromazine but not affected by mephenesin, could be re-activated by small doses of strychnine (0.1 mg/kg) in the presence of chlorpromazine. This reactivated discharge was then abolished by the same dose of mephenesin as had previously been ineffective against the γ-discharge (Fig. 6).

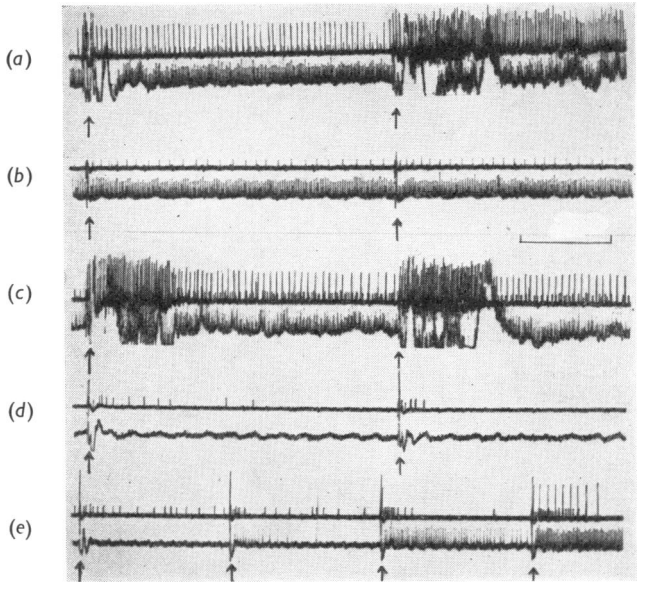

Fig. 4. Ventral root records from decerebrate rabbit with local tetanus. The upper tracing is from a root filament on the affected side and the lower tracing is from the unaffected side. Note the greater α-activity on the tetanus side. Stimuli were applied to the sural nerve on the unaffected side. (*a*) Control activity showing response to stimuli; muscle contraction caused a relatively slow deflection of the lower beam due to displacement of the recording electrodes. (*b*) After mephenesin (20 mg/kg) all α-activity was abolished as well as the muscle contraction, but γ-activity persisted although reduced. (*c*) Control activity. (*d*) After chlorpromazine (0.5 mg/kg) all reflex and α-activity was abolished and γ-activity was only obtained after stimulation. (*e*) γ-Activity (and some α-) was returning 45 min after chlorpromazine.

Some observations were also made of the effect of mephenesin on stretch-induced α-discharges. If mephenesin does not block the monosynaptic reflex then it should not affect the response of the α-motoneurone to stretch of its own muscle. This was found to be so in the experiment shown in Fig. 7. Mephenesin abolished the tonic ventral root recorded α-discharge but not the γ-activity. Stretch of the medial gastrocnemius muscle still produced an α-discharge as in the control, although there was no maintained activity. Rather surprisingly in two other similar experiments it was found that mephenesin also abolished the stretch-induced α-activity. The problem clearly requires further investigation.

Muscle spindle activity

The discharge frequency of a muscle spindle depends on two main factors; the stretch or tension imposed upon it and its state of excitability as determined by the γ-innervation. Thus at any given tension (more correctly, extrafusal muscle fibre length) the spindle discharge is always greater when the γ-innervation is active than when the spindle has been denervated. This difference in discharge between the innervated and denervated spindle is an indication of the degree of γ-activity or γ-bias. Thus, if the discharge of the innervated spindle is recorded at different tensions before and after a drug, then any difference in

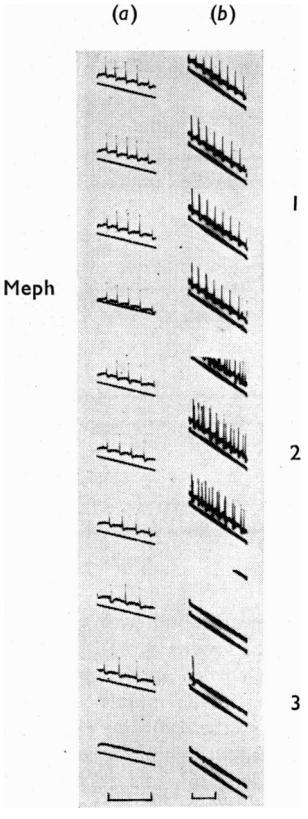

Fig. 5. Tonic α-motoneurone discharge in a ventral root filament of a decerebrate rabbit. Sweeps at 1-sec intervals. In (*a*) an intravenous injection of mephenesin (20 mg/kg), started at Meph, abolished the discharge before the injection was completed. In (*b*) chlorpromazine (0.5 mg/kg) produced a characteristic initial increase in discharge (2) over the control level (1) and did not become fully effective for 4 min (3). Time calibrations, 0.5 sec.

discharge frequency indicates either depression of the γ-influence on the spindle or a direct effect on the spindle itself. The latter possibility was eliminated by testing the drugs on spindles which had been denervated (de-efferented) by cutting the appropriate (L6 to S3) ventral roots. Spindle discharge frequencies were taken from the frequency integrator and displayed on a pen oscillograph (Fig. 8). Peak and adapted discharges were read off and plotted against muscle tension or weight stretching the muscle. Units were taken from both plantaris and gastrocnemius medialis.

Mephenesin depressed the innervated spindle slightly (Fig. 9,*a*) but had no effect after denervation. On the other hand, chlorpromazine produced a considerable depression of both the innervated spindle peak and adapted discharges (Fig. 9,*b*) but had no effect after denervation (Fig. 10). Thus chlorpromazine has a marked, and mephenesin a slight, effect on γ-activity but neither drug affected the spindle directly in the doses used. This also

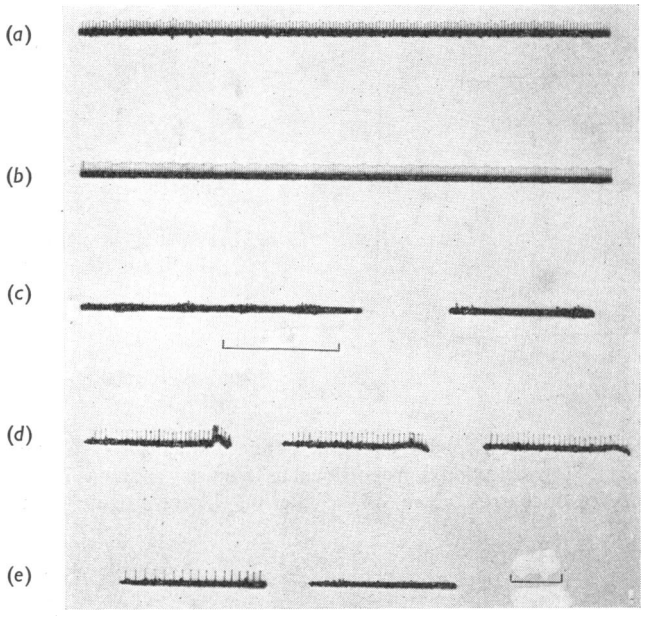

Fig. 6. Single γ-unit recorded from a ventral root filament of a decerebrate rabbit. (*a*) Control discharge; (*b*) discharge increased by 20 mg/kg of mephenesin; (*c*) chlorpromazine, 1.0 mg/kg, abolished activity; (*d*) strychnine, 0.1 mg/kg given 10 min after chlorpromazine, restored firing; and (*e*) this discharge was abolished by the previously ineffective dose of mephenesin. The upper time calibration is 1 sec and applies to (*a*), (*b*) and (*c*); the lower time calibration is 0.2 sec and applies tc (*d*) and (*e*).

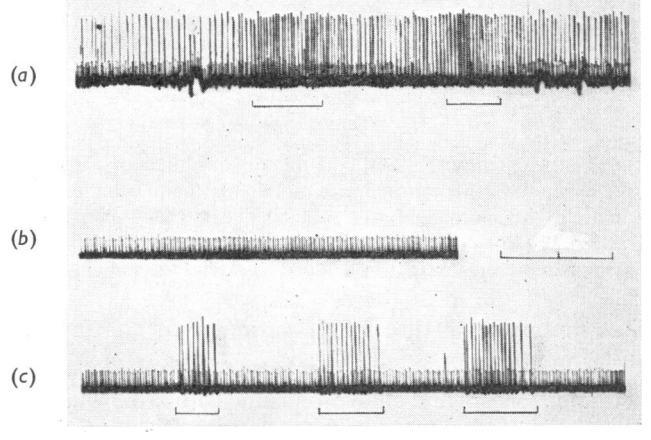

Fig. 7. Effect of mephenesin on stretch-induced α-discharge recorded in the ventral root of a decerebrate rabbit. Tonically firing α- and γ-units are shown in (*a*) as well as the increased discharge of the α-unit on stretch of the gastrocnemius muscle during horizontal lines. After mephenesin (20 mg/kg), tonic α-firing ceased (*b*), but stretch still induced reflex activity (*c*). Stimuli applied to the gastrocnemius nerve produced evoked spikes identical to those obtained by muscle stretch.

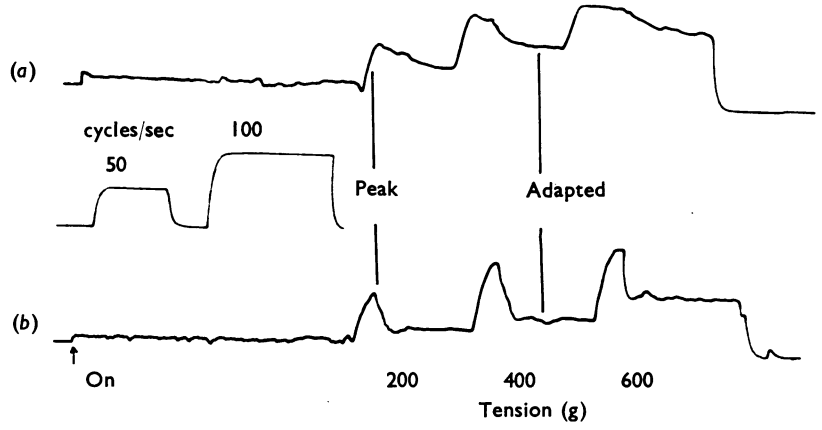

Fig. 8. Pen oscillograph record of a spindle discharge obtained when increasing weights (tension) were applied to the muscle. The deflection is proportional to frequency as shown by the calibration tracing. Both peak and adapted discharges before (*a*) and after (*b*) chlorpromazine (0.5 mg/kg) are shown.

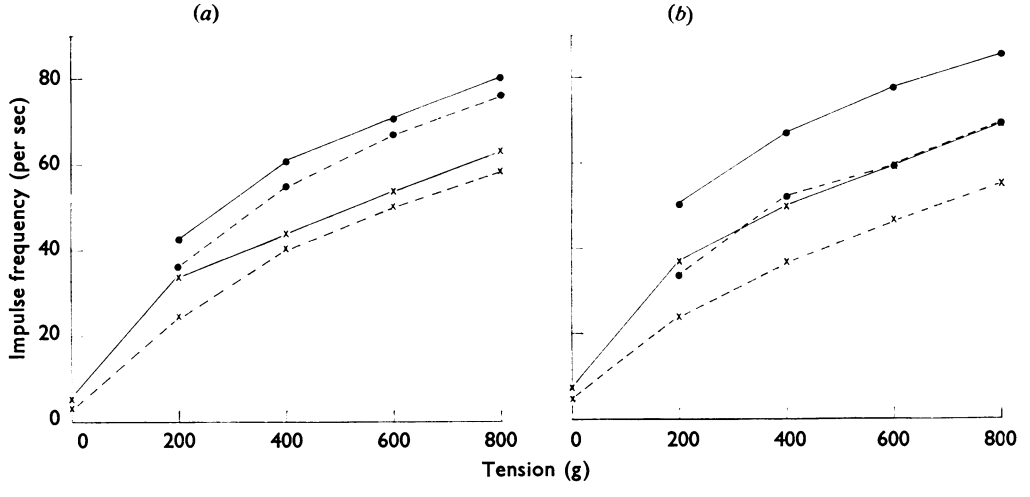

Fig. 9. Effect of 20 mg/kg of mephenesin (*a*) and 0.25 mg/kg of chlorpromazine (*b*) on tension/discharge curves of rabbit muscle spindles. Mean results are plotted for eleven spindles from either the plantaris or gastrocnemius muscles of six decerebrate rabbits. Peak (●——●) and adapted (×——×) discharges before, and peak (●- - -●) and adapted (×- - -×) discharges after, drug administration are shown. The abscissa represents weight in g added to extend the muscle.

supports the previous finding from direct observations that chlorpromazine produces a marked depression of γ-motoneurones.

The relative effect of mephenesin and chlorpromazine compared with that of de-efferentation was tested on spindle activity as shown in Fig. 11. Chlorpromazine in the dose used (0.25 mg/kg) did not completely block γ-activity but is obviously much more effective than mephenesin. Although chlorpromazine seems from Fig. 9,*b* to depress equally peak and adapted spindle discharges it would appear from Fig. 8 that, in the absence of γ-innervation, following chlorpromazine, the spindle discharge adapts much more rapidly.

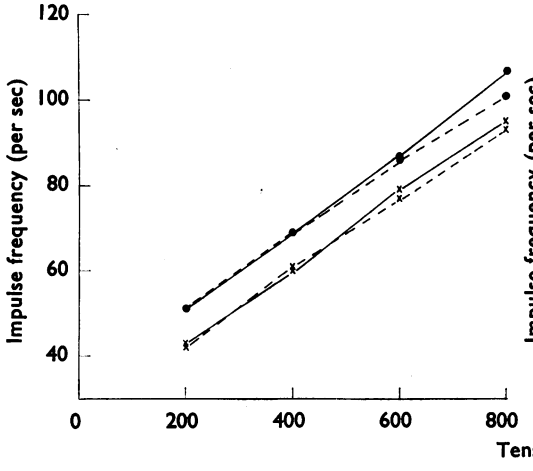

Fig. 10. Effect of chlorpromazine on discharge of seven de-efferented spindles from plantaris or medial gastrocnemius muscles of three decerebrate rabbits. Peak (●——●) and adapted (×——×) discharges before chlorpromazine (0.25 mg/kg) and peak (●- - -●) and (×- - -×) adapted afterwards are shown.

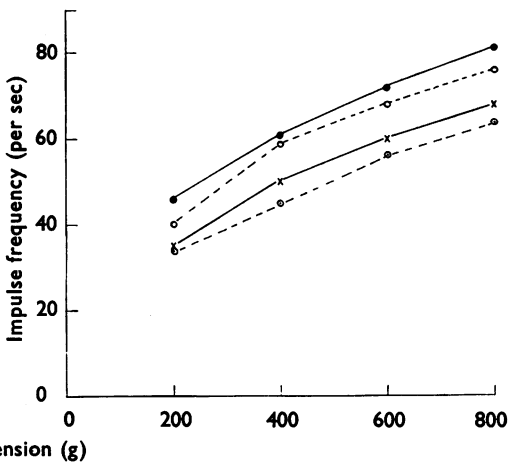

Fig. 11. Mean discharge of seven muscle spindles from plantaris or gastrocnemius muscles of four decerebrate rabbits before control ●——●, and after mephenesin (20 mg/kg) O- - -O, chlorpromazine (0.25 mg/kg) ×——×, and de-efferentation ⊙- - -⊙. Averages of the peak and adapted discharges are shown. The abscissa shows weight in g used to extend the muscle.

The conduction velocities of the spindles studied ranged from 39 to 100 m/sec. Two-thirds were primary fibres, that is having a conduction velocity above 67 m/sec. Although no systematic attempt was made to look for a differential drug effect on the two types of units, it appeared that both were equally affected by chlorpromazine.

DISCUSSION

Mephenesin and chlorpromazine are both known to produce muscular relaxation in the conscious rabbit, but certain differences in the manner in which they achieve this effect (Webster, 1961) prompted an investigation into their relative effectiveness against α- and γ-motoneurone activity at dose levels which produce equivalent muscular relaxation. Records from motor nerve and ventral root filaments showed that both mephenesin and chlorpromazine depressed α-motoneurones in the decerebrate rabbit although mephenesin was slightly more effective in this respect that chlorpromazine. On the other hand, chlorpromazine depressed the γ-motoneurone considerably more than did mephenesin. The depression of γ-motoneurones by chlorpromazine has previously been shown in the decerebrate cat by Henatsch & Ingvar (1956) and Busch, Henatsch & Schulte (1960) but neither group of workers reported any effect of chlorpromazine on the α-motoneurone other than a change in the tonic stretch reflex response of this neurone to a phasic response. Henatsch & Ingvar (1956), however, used cats decerebrated by the anaemic method of Pollock & Davis (1930), in which rigidity is maintained by α-activity, and their results are probably therefore not comparable. Since in our preparations both tonic and reflex-

induced α-discharges were abolished by chlorpromazine, it cannot be concluded that chlorpromazine has no effect on the α-motoneurone as proposed by Henatsch & Ingvar (1956) and Hudson & Domino (1963).

Muscle relaxation produced by mephenesin could be due either to a direct depression of the α-motoneurone or to a reduction in its excitability by removal of interneuronal influences. The former seems unlikely since mephenesin does not abolish all voluntary movement, and the monosynaptic stretch reflex has generally been found to be unaltered. A maintained α-discharge to muscle stretch after mephenesin was in fact observed in some experiments although it did not occur consistently (Fig. 7). The possibility remains that stretch-induced monosynaptic discharges are conveyed to the motoneurone by synaptic contacts that are unaffected by mephenesin whilst it blocks all other pathways to the motoneurone at the neurone and not at interneurones. If mephenesin blocked transmission at interneurones as suggested by Longo (1961) it would not be expected to leave γ-discharges relatively unaffected as the reticular control over this system appears to be carried over polysynaptic pathways (Diete-Spiff, Dodsworth & Pascoe, 1962).

Chlorpromazine probably causes a reduction in muscle tone by primarily abolishing γ-motor nerve activity and thus reducing the afferent input into the cord from the muscle spindles. This would automatically reduce the excitability of the α-motoneurones. However, some direct cord or supraspinal effect on the α-neurone probably occurred since not only was tonic α-activity abolished in many cases, but the response to afferent stimulation was often completely counteracted (Figs. 2, 3 and 4). If chlorpromazine had no effect on the motoneurone other than by the depression of the afferent spindle input it should not affect ventral root discharges after the afferent input has been abolished by appropriate dorsal root or motor nerve section. But our experiments showed that in dorsal root preparations, in which motor nerves had been extensively sectioned and the afferent input therefore considerably reduced, chlorpromazine remained effective against ventral root discharges. Chlorpromazine also retained an effect on α-discharges after the preparation of a number of ventral roots for recording, which automatically cuts down the γ-influence to the spindles, and after the splitting down of the motor nerve which greatly reduces the afferent input to the cord. The observations by other workers that chlorpromazine can reduce dorsal root or motor nerve evoked reflex discharges (Hudson & Domino, 1963) when presumably some of the afferent input must have been reduced by the requirements of the preparation also implies a direct effect of chlorpromazine on the α-system. Nevertheless, the main effect of chlorpromazine is presumably a depression of the γ-motor system. Some initial stimulation, particularly of α-motoneurones, was noted after chlorpromazine (Fig. 5).

Another difference between the central actions of chlorpromazine and mephenesin is that chlorpromazine has less antistrychnine activity (Meidinger, 1956; de Silva & Evans, 1960). This difference can also be shown on γ-motor nerve activity. A γ-unit which is unaffected by mephenesin but depressed by chlorpromazine can be reactivated by strychnine in the presence of chlorpromazine and this strychnine-activated discharge is then sensitive to mephenesin (Fig. 6). Whether this is a cumulative depressant effect of chlorpromazine and mephenesin or whether it depends on strychnine activating some central elements which drive the γ-neurones and are sensitive to mephenesin but not chlorpromazine is uncertain.

Observations of muscle spindle discharges confirmed the depressant effect of chlorpromazine on γ-activity and showed that neither mephenesin nor chlorpromazine had any direct effect on the denervated spindle. The possibility that in addition to their effect on the γ-motoneurone both mephenesin and chlorpromazine could modify the effect of this system at the spindle under normal conditions has not been eliminated.

It is interesting that there was no differential effect of chlorpromazine on the peak and adapted spindle discharges (Fig. 9, *b*), although there was some suggestion that the spindle adapts more rapidly after chlorpromazine (Fig. 8). It should be pointed out that no attempt was made to distinguish between the effect of drugs on primary and secondary spindle afferents. This should not have introduced a serious error, however, since Harvey & Matthews (1961) have shown that extension-frequency curves, such as those used in the present studies, are similar for both afferent endings and that γ-bias only alters the level and not the slope of such curves. Nevertheless the presence of two types of spindle afferents as well as the fact that there are probably more than one form of γ-fibre should be taken into account in future studies.

Drugs, such as chlorpromazine, that depress the γ-motor system should be useful muscle relaxants, particularly if this effect is relatively specific, and tests of the type outlined above can be valuable. Complete depression of spindle activity by a direct action may not be desirable, since the compound 2,4-di(diethylamino)-6-(2-phenylacetylhydrazino)-1,3,5-triazine (Ciba 28882BA), although shown by Bein & Fehr (1962) to produce a considerable direct depression of the muscle spindle in the cat, does not produce a comparable muscular relaxation in the rabbit (unpublished observations). A drug with a specific effect on γ-activity may be more useful.

Since muscle tone is maintained by the stretch reflex any reduction in the intensity of this monosynaptic reflex should produce muscular relaxation. It is particularly interesting therefore that mephenesin, generally considered to be the standard for centrally acting muscle relaxants, achieves muscular relaxation by depression of polysynaptic activity. It appears to depress the α-motoneurone by removal of interneurone excitatory drive without any great effect on the monosynaptic reflex. Perhaps the time has come when centrally acting muscle relaxants should be evaluated by studying changes in the electromyogram and in the discharge of α- and γ-motoneurones.

SUMMARY

1. The effect of mephenesin and chlorpromazine has been studied on α- and γ-motor nerve activity recorded in ventral root and motor nerve filaments of decerebrate rabbits.

2. Mephenesin (20 mg/kg) produced a marked depression of α-activity but was relatively ineffective against γ-discharges.

3. Doses of chlorpromazine (0.25 to 0.5 mg/kg) which were known to produce the same muscular relaxation as 20 mg/kg of mephenesin abolished most γ-activity besides greatly reducing the discharge of α-motoneurones.

4. Studies of the discharge frequency of both innervated and denervated muscle spindles at various muscle tensions showed that neither drug had any direct effect on the spindle but confirmed the depression by chlorpromazine of γ-activity.

5. The significance of these results is discussed in relation to the muscular relaxation produced by both drugs.

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