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ELECTRICAL RESPONSES OF CAT SUPERIOR CERVICAL GANGLIA IN VIVO TO SOME STIMULANT DRUGS AND THEIR MODIFICATION BY HEXAMETHONIUM AND HYOSCINE

BY

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In a previous paper (Brown, 1966) some effects of hexamethonium and hyoscine on drug-induced depolarization of isolated superior cervical ganglia were described. The results suggested that, with different depolarizing agents, ganglionic depolarization could be described as either a nicotinic type of action, or a muscarinic action, or a combination of both actions.

The present experiments were undertaken to find out if the responses of superior cervical ganglia *in vivo* to stimulant drugs showed similar characteristics to those seen *in vitro*. For this purpose, changes of ganglionic potential and postganglionic nerve discharges following intra-arterial injections of stimulant drugs have been recorded simultaneously. Some previous observations using this method of recording have been reported by Volle and his associates (Takeshige, Pappano, DeGroat and Volle, 1963; Takeshige & Volle, 1964a, b, c and d. The experimental technique used in the present investigation differed slightly from that employed by these workers in that the potentials have been recorded from the internal carotid branch of the postganglionic cervical sympathetic nerve (which innervates the orbit) instead of from the finer external carotid branch.

METHODS

Experiments were performed in 19 cats anaesthetized with sodium pentobarbitone (35 mg/kg intraperitoneally). Dissection of the pre- and post-ganglionic cervical sympathetic nerves, and of the lingual artery for injection, was carried out as described previously (Brown & Quilliam, 1964a). The pre- and post-ganglionic nerves were sectioned acutely, the latter as near its point of entry into the skull as possible, and saline-soaked cotton threads tied to the cut ends.

Changes of ganglionic potential were recorded using two non-polarizable Ag/AgCl/saline-agar electrodes, fitted with balsa-wood wicks soaked in a 2% solution of agar in saline. One electrode was placed on the body of the superior cervical ganglion, near the point of entry of the preganglionic nerve trunk; the other was placed on the junction between the saline-soaked cotton thread and the end of the postganglionic nerve trunk. The two electrodes were connected through a direct-coupled preamplifier to the upper (Y_1) beam of an oscilloscope, providing 1 cm vertical deflection of the electron beam/200 μV potential change (ganglionic negativity upwards).

Electrical activity in the postganglionic nerve trunk was recorded by looping a shielded platinum electrode round the postganglionic trunk, stripped of its sheath but otherwise intact, about 2 to 3 mm from the ganglion. The circuit was completed using the Ag/AgCl electrode on the end of the postganglionic nerve as the second recording electrode. This arrangement was used because the short postganglionic nerve (about 0.5 to 1 cm) left little room for bipolar platinum electrodes. Introduction of the platinum electrode altered the resting potential difference recorded between the two Ag/AgCl electrodes, but did not lead to fluctuations in that potential difference, nor did it modify the changes of ganglionic potential elicited by test injections of carbachol or potassium chloride. Postganglionic nerve activity was amplified by two condenser-coupled amplifiers in cascade (gain, 3 db down at 35 and 2,000 cycles/sec), and displayed on the lower (Y_2) beam of the oscilloscope at a magnification of about 10 μV/cm (noise level and interference, about 2 to 5 μV). Both ganglionic potentials and postganglionic nerve activity were photographed on moving film (speed, 3 in/min).

When required, the preganglionic cervical sympathetic nerve was stimulated through bipolar platinum electrodes with single shocks of 0.1 msec duration, delivered from an electronic stimulator through an isolating transformer. Evoked ganglionic action potentials were recorded on the upper beam of the oscilloscope using the two Ag/AgCl recording electrodes, and were photographed on stationary film.

During recording, the cat was placed in an earthed metal box. The cat itself was not earthed, being insulated from the metal box, but the distal Ag/AgCl electrode was earthed. The nerves were immersed in a pool of liquid paraffin, warmed to 35 to 37° C with a lamp, and previously equilibrated with saline.

Drugs, dissolved in 0.2 ml. of 0.9% saline solution, were injected retrogradely into the lingual artery while the external carotid artery was occluded. Injections were made from a hand-operated tuberculin syringe attached through fine polythene tubing to a cannula in the stump of the lingual artery (dead space, 0.06 ml). Injection took 3 to 4 sec. By firmly clamping the syringe to an upright bar and insulating the operator's (earthed) hand from the syringe plunger, injection artefacts obtained with control saline injections were limited to at most a small (20 to 50 μV) positive DC potential shift. Stimulant drugs were routinely administered at 15 min intervals, and were preceded each time by a control saline injection. Since the time-course and amplitude of the responses to carbachol varied quite considerably in different experiments, the effects of other stimulant drugs were nearly always compared directly with those of carbachol in the same cat.

The following drugs were used: acetylcholine chloride, carbachol chloride, nicotine hydrogen tartrate, tetramethylammonium bromide, synthetic dl-muscarine iodide, potassium chloride, hexamethonium bromide, and hyoscine hydrobromide. Doses refer to the weight of salt injected in 0.2 ml. of saline (intra-arterially), or in 0.5 ml. of saline if given intravenously (through a cannula in the femoral vein).

RESULTS

Ganglionic potentials and postganglionic nerve activity

Carbachol.—Effects of intra-arterial injections of carbachol were recorded in 19 cats. Some responses to carbachol are shown in Figs. 1 and 2, and also in Figs. 3, 4 and 5.

Doses of carbachol between 1 and 3 μg produced a slow negative shift in the resting potential difference between the surface of the ganglion and the cut end of the postganglionic nerve trunk, lasting 30 sec or more (see Fig. 1, upper beam). Doses above 3 μg sometimes evoked a negative ganglionic potential of larger amplitude (Fig. 3), but more frequently (11 out of 17 experiments) elicited a complex sequence of ganglionic potential changes, consisting of an initial negative deflection, followed by a dip or a reversal to a ganglionic positivity, and then a second sustained negative shift (Fig. 1). In two experiments, with doses of 5 and 10 μg, no initial negative deflection occurred;

instead, a slow positive shift immediately succeeded the injection, followed by the late negative potential. Sometimes with repeated injections of the same dose of carbachol the response slowly changed from a simple ganglionic negative potential to the more complex sequence of changes described above.

Ganglionic potential changes were accompanied by an asynchronous discharge of action potentials recorded in the postganglionic nerve trunk (Fig. 1, lower beam). The amplitude and duration of the discharge increased smoothly with increasing doses of

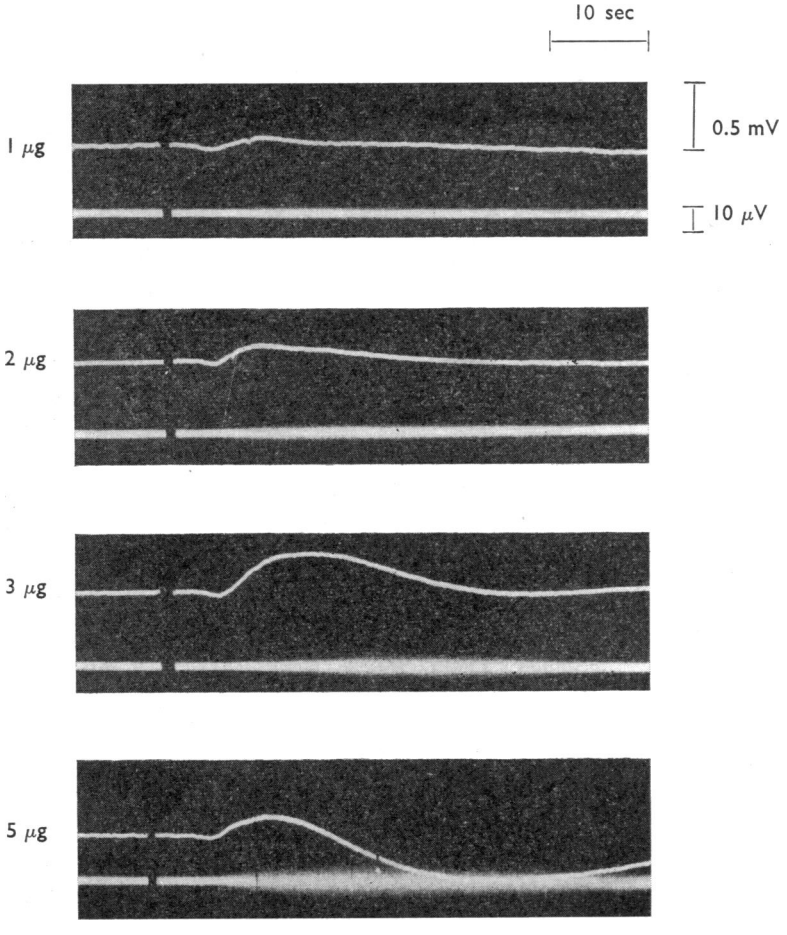

Fig. 1. Changes of the potential difference between the surface of the superior cervical ganglion and the cut end of the postganglionic (internal carotid) cervical sympathetic nerve trunk (upper traces, ganglionic negativity upwards), and asynchronous discharges of action potentials recorded from the postganglionic nerve trunk (lower traces) following intra-arterial injections of 4 increasing doses of carbachol to the superior cervical ganglion of an anaesthetized cat. Carbachol was injected retrogradely into the lingual artery while the external carotid artery was occluded. Injection commenced at the break in the records and occupied 3 to 4 sec. Injections were made at 15 min intervals. Doses refer to the weight of carbachol injected in 0.2 ml of saline. The records were taken on moving film, and read from left to right.

carbachol. Though the discharge usually began during the initial negative ganglionic potential (except in the two experiments where this was absent, when it commenced during the positive shift), the discharge persisted without modification during subsequent positive swings of ganglionic potential. The amplitude of the discharge recorded in these experiments (not usually more than 10 to 20 μV) appears to be rather less than that reported by Takeshige and Volle (1964a, b, c and d). This could be accounted for either by a less synchronous discharge or by the greater thickness of the internal carotid branch of the postganglionic nerve. In either case there might be more shunting of activity in discharging fibres through adjacent inactive fibres. In some experiments where the discharge was exceptionally small, it was increased in amplitude by splitting the postganglionic trunk into its constituent rami and looping the electrode round only one of the rami.

Hexamethonium (100 μg intra-arterially; eight experiments) reduced the negative ganglionic potential evoked by carbachol, and reduced, but did not usually abolish, the

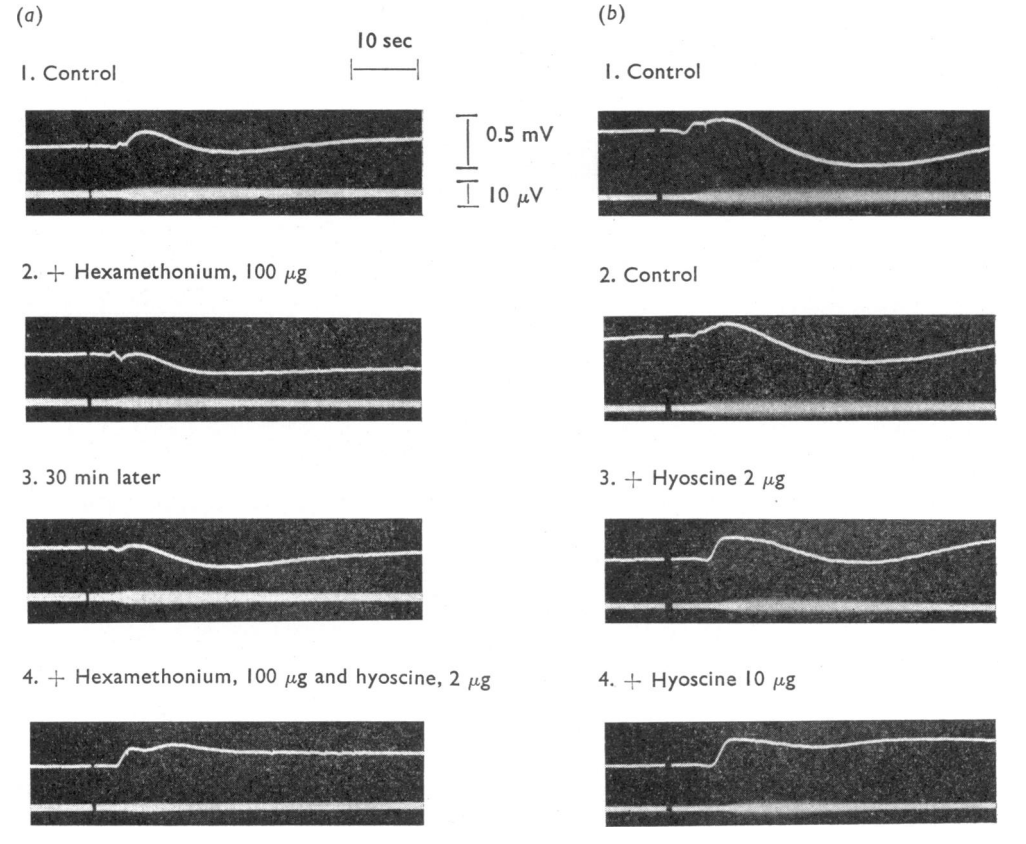

Fig. 2. Effects of (*a*) hexamethonium and hexamethonium with hyoscine, and (*b*) hyoscine alone on the ganglionic potential changes and postganglionic nerve discharges produced by intra-arterial injections of 5 μg of carbachol to the superior cervical ganglion (two experiments). Blocking agents were injected intra-arterially 1 min before the injection of carbachol. Other carbachol injections were preceded by control saline injections.

postganglionic discharge (Fig. 2,*a*). The positive ganglionic potential was not reduced, but rather enhanced, by hexamethonium. Increasing the dose of hexamethonium to 1 mg further reduced ganglionic negativity and discharge, but still did not affect the positivity.

Hyoscine (2 μg and 10 μg intra-arterially, eight experiments; or 0.5 mg/kg intravenously, two experiments) invariably increased the height of the negative ganglionic potential produced by carbachol, and reduced or abolished the ganglionic positivity (Fig. 2,*b*). Hyoscine also impaired the postganglionic nerve discharge produced by carbachol: the effect of hyoscine on the duration of the discharge was particularly noticeable (Fig. 2,*b*). In contrast to the effect of hexamethonium which lasted only 15 min or so, the action of hyoscine was very long-lasting and could be detected an hour or more after a single intra-arterial injection (see Fig. 5).

The effects of a combination of hexamethonium (100 μg) with hyoscine (2 μg) on the ganglionic potential changes evoked by carbachol resembled more closely those seen with hyoscine alone, rather than those observed with hexamethonium: thus the ganglionic negativity was increased and the positivity reduced (Fig. 2,*a*). The postganglionic nerve discharge was inhibited more completely by hexamethonium and hyoscine in combination than by either agent separately.

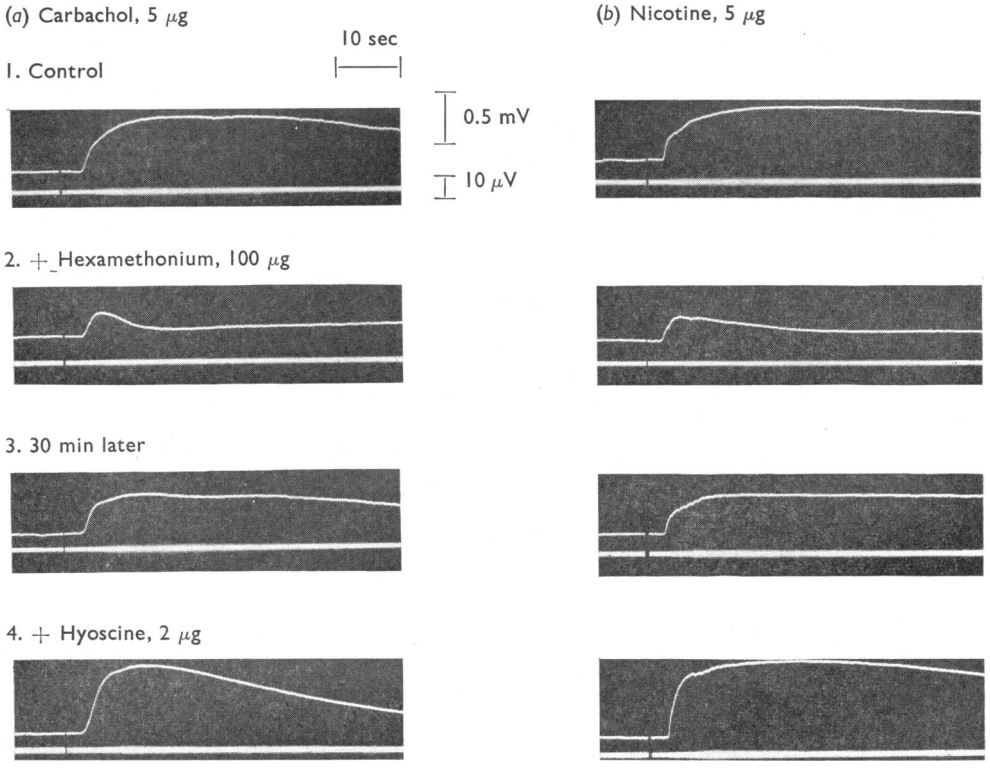

Fig. 3. Effects of intra-arterial injections of hexamethonium and hyoscine on the ganglionic potentials and postganglionic nerve discharges elicited by alternate intra-arterial injections of (*a*) carbachol and (*b*) nicotine to the superior cervical ganglion of an anaesthetized cat.

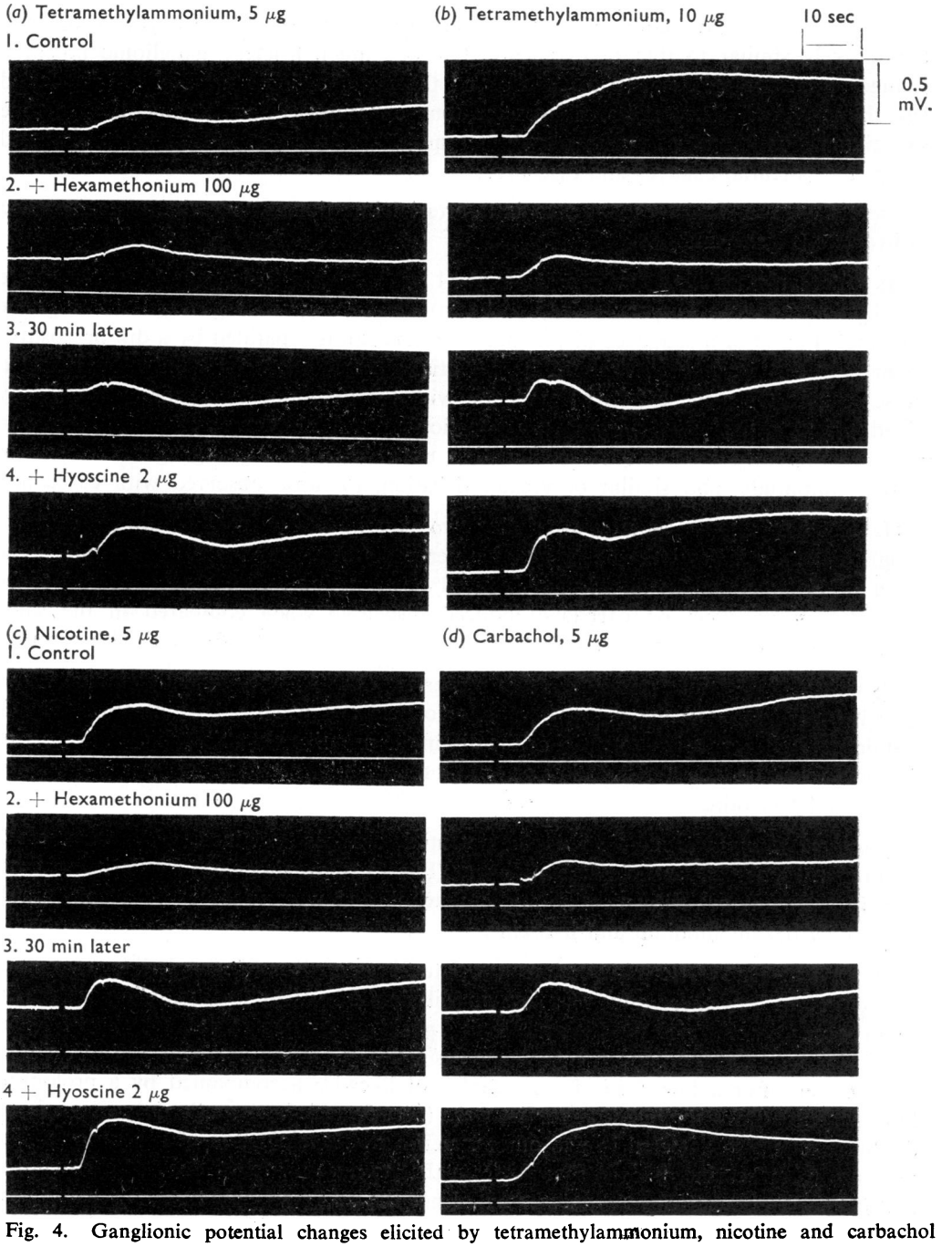

Fig. 4. Ganglionic potential changes elicited by tetramethylammonium, nicotine and carbachol injected intra-arterially at 15 min intervals to the superior cervical ganglion of an anaesthetized cat, and effects of intra-arterial injections of hexamethonium and hyoscine on these potentials. (In this experiment, postganglionic nerve activity could not be recorded because of a fault in the electronic recording apparatus.)

Acetylcholine.—The action of acetylcholine (10 to 100 μg; three experiments) was qualitatively similar to that of carbachol, but was much briefer: ganglionic potential changes were complete by 10 to 30 sec and the postganglionic nerve discharge lasted less than 10 sec. The effects of hyoscine (one experiment) and hexamethonium (one experiment) on these responses closely resembled their effects on carbachol-induced ganglionic potential changes and discharge.

Nicotine.—Ganglionic responses to intra-arterial injections of nicotine were recorded in five cats (Figs. 3 and 4).

As with carbachol, low doses of nicotine (1 or 2 μg) produced a prolonged negative ganglionic potential. Larger doses (5 or 10 μg) elicited either a large amplitude negative potential (Fig. 3) or a sequence of two negative deflections separated by a dip or positive swing (Fig. 4). In each experiment the potential changes produced by nicotine reflected those seen in the same cat with carbachol, with the exception that those produced by nicotine were rather more prolonged. Ganglionic potential changes elicited by nicotine were accompanied by a discharge of action potentials in the postganglionic trunk of similar amplitude, and similar or greater duration, to those observed with carbachol.

Hexamethonium (100 μg intra-arterially; two experiments) depressed both the negative ganglionic potential and the postganglionic nerve discharge produced by nicotine. The effect of hexamethonium on nicotine-induced postganglionic discharge appeared to be greater than its effect on carbachol-induced discharge when compared in the same experiment. Hexamethonium enhanced the dip or positive shift observed with nicotine.

Hyoscine (2 μg intra-arterially, two experiments; 0.5 mg/kg intravenously, two experiments) enhanced the negative ganglionic potential produced by nicotine (Fig. 3) and depressed the positive potential or the dip in the negative potential (Fig. 4). Hyoscine did not clearly reduce the duration or amplitude of the postganglionic nerve discharge produced by nicotine.

Tetramethylammonium.—Ganglionic potential changes obtained with tetramethylammonium, recorded in a single experiment (Fig. 4), showed a close similarity to those seen in the same cat with nicotine and carbachol, and were modified in a comparable manner by hexamethonium and hyoscine.

Muscarine.—Intra-arterial injections of 0.5 to 20 μg of dl-muscarine iodide were made in 4 cats. In 3 of these only very low amplitude (150 μV or less) ganglionic potential changes were seen, once negative and twice positive. In the fourth cat, 1 to 5 μg of muscarine repeatedly produced a prolonged negative deflection of about 300 μV, similar to that seen after a low dose of carbachol, and likewise accompanied by a prolonged, low-amplitude postganglionic nerve discharge (Fig. 5). (A low-amplitude postganglionic discharge was also detected in one other experiment after injection of muscarine.) The response to muscarine differed sharply from that to an equi-active dose of carbachol in that neither the negative ganglionic potential nor the postganglionic nerve discharge were reduced by hexamethonium, but both were abolished by hyoscine.

Potassium chloride.—In each of 7 cats, injections of 0.5 to 2 mg of potassium chloride produced a large, simple negative ganglionic potential, the size of which increased sharply to a level of about 1 to 2 mV as the dose of potassium chloride was increased

by 0.5 mg steps (Fig. 6). There was never any pronounced dip or positive potential shift to interrupt the slow negative potential, even in experiments where other drugs produced complex potential changes with a pronounced positive swing. The amplitude of the postganglionic nerve discharge produced by potassium chloride was similar to that seen with carbachol, but discharge did not appear until higher levels of ganglionic negativity were attained. Potassium chloride-induced postganglionic discharge was brief (usually less than 15 sec in duration) and ceased while the ganglionic negativity was still pronounced. Neither hexamethonium (100 μg and 1 mg; one experiment), nor hyoscine (2 and 10 μg; three experiments) noticeably affected the ganglionic negativity or postganglionic nerve discharge produced by potassium chloride.

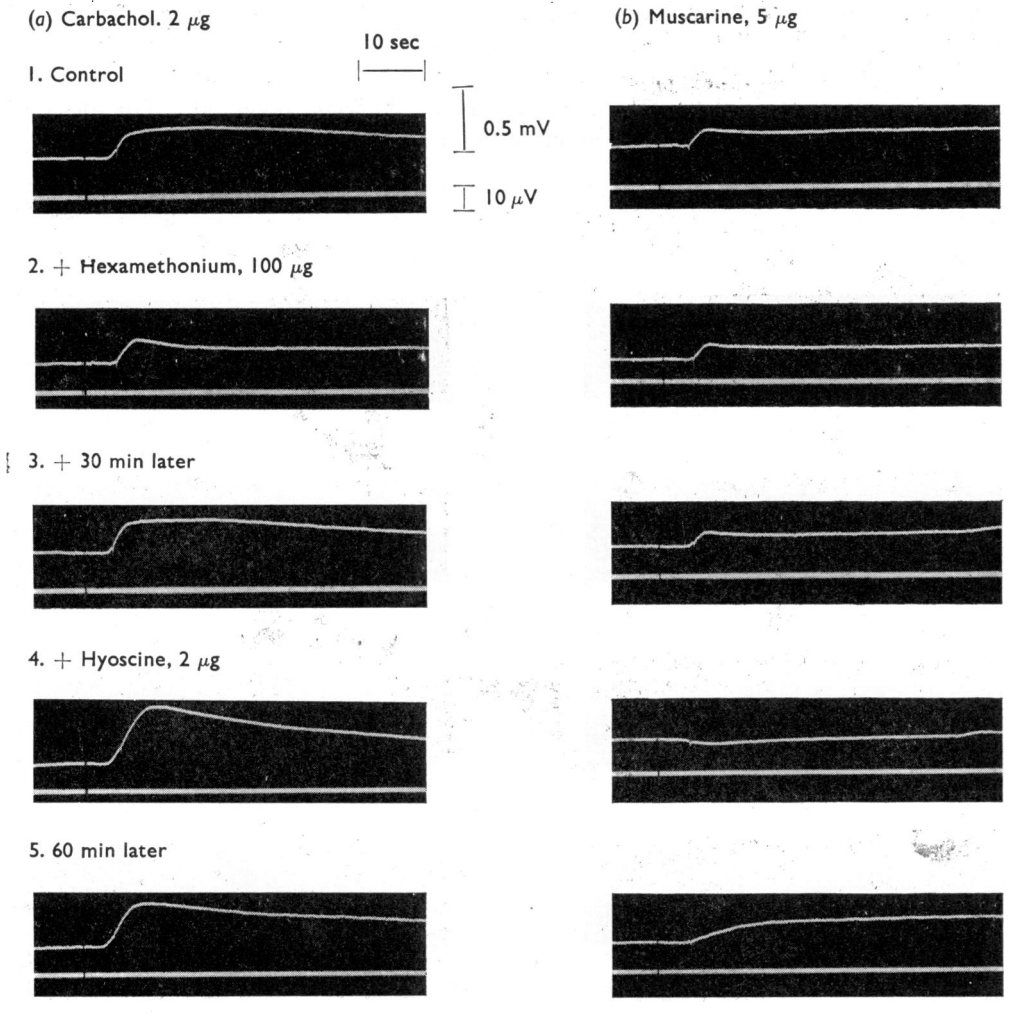

Fig. 5. Effects of intra-arterial hexamethonium and hyoscine on the ganglionic potential changes and postganglionic nerve discharges elicited by alternate intra-arterial injections of equi-effective doses of carbachol and dl-muscarine to the superior cervical ganglion of an anaesthetized cat.

Evoked ganglionic action potentials

The ganglionic action potential recorded in response to single maximal shocks applied to the preganglionic nerve consisted of the usual spike potential (0.5 to 1 mV negative), a short negative after potential, and a large slow positive after-potential (P-wave, 0.4 to 0.8 mV) (Fig. 7, frame 1). The size and duration of the components of the ganglionic action potential varied from experiment to experiment, but remained fairly constant in each experiment.

Hexamethonium (20 μg intra-arterially) strongly reduced all the components of the action potential. After 100 μg no action potential could be discerned (two experiments).

Hyoscine (2 μg intra-arterially; three experiments) either did not affect or slightly increased the height of the spike potential. Hyoscine consistently reduced the size of the P-wave by between 30 and 45% (Fig. 7, frames 2 to 4). No effect on the size of the negative after-potential was seen, though, probably because the P-wave was reduced, the negative after-potential took off from a higher ganglionic potential. The effect of hyoscine on the P-wave persisted for about an hour after a single injection.

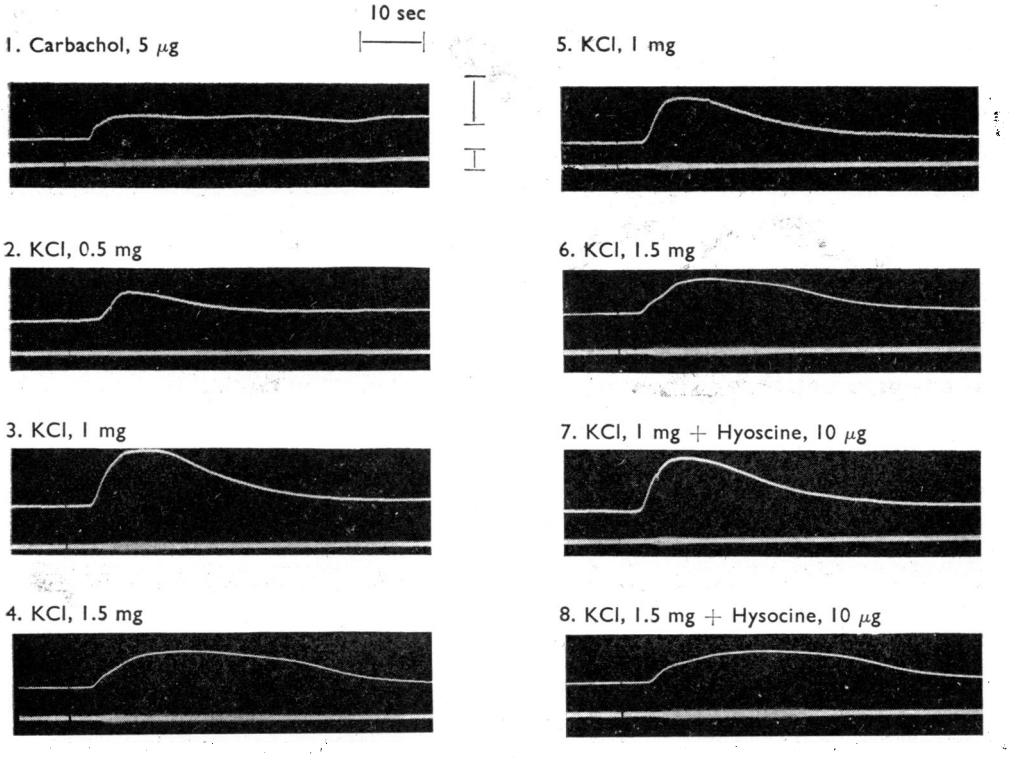

Fig. 6. Ganglionic potential changes and postganglionic nerve discharges evoked by intra-arterial injections of carbachol (frame 1), and potassium chloride (frames 2 to 8) to the superior cervical ganglion of an anaesthetized cat. Note that the upper vertical calibration indicates 0.5 mV ganglionic potential change for frames 1, 2, 3, 5 and 7, and 1.5 mV potential change for frames 4, 6 and 8. Lower calibration, 10 μV throughout.

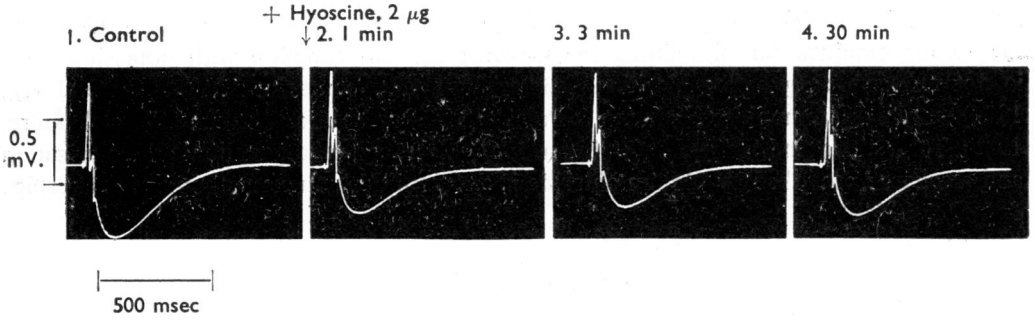

Fig. 7. Ganglionic action potentials recorded in response to single maximal shocks (0.1 msec duration; 5/min) applied to the preganglionic cervical sympathetic nerve (1) 1 min before and (2), (3) and (4), 1, 3 and 30 min after the intra-arterial injection of 2 μg of hyoscine to the superior cervical ganglion. (Retouched.)

DISCUSSION

The nature of the ganglionic potential changes produced by stimulant drugs, and the effects of hexamethonium and hyoscine on these potential changes and on the postganglionic nerve discharges, are summarized in Table 1. Although only a limited number of experiments have so far been done (particularly with muscarine and tetramethylammonium), certain clear similarities and differences between the responses to the different drugs have emerged, from which a provisional classification of the drugs into three groups may be made.

Group A. (*Carbachol, acetylcholine, nicotine and tetramethylammonium*).—These drugs produced either a simple negative ganglionic potential or a sequence of negative-positive-negative potential changes, depending to a large extent on the dose. Both the negative ganglionic potentials and the postganglionic nerve discharges were reduced by hexamethonium, which implies a primarily nicotinic action. The appearance of the positive potentials, which were not affected by hexamethonium, and the effects of hyoscine on the responses, suggest some additional action or actions, which are discussed below.

Group B. (*Muscarine*).—The low amplitude of the ganglionic potentials and postganglionic nerve discharges elicited by muscarine made analysis difficult. However, in one cat muscarine produced a sufficiently large and consistent negative ganglionic potential to permit comparison with carbachol, from which it was seen that the response to muscarine showed considerable differences from that to carbachol: neither ganglionic negativity nor postganglionic nerve discharge were affected by hexamethonium, whereas both were abolished by hyoscine. This finding accords with previous reports (see Brown, 1966, for references) that the ganglion-stimulant action of muscarine is not a nicotinic side-effect but an unconventional example of its conventional muscarinic action. The findings of Takeshige *et al.* (1963) indicate that methacholine also belongs to this group of muscarinic ganglion stimulant agents.

Group C. (*Potassium chloride*).—This agent evoked a large, simple ganglionic negative potential and a brief postganglionic nerve discharge, neither of which were affected by hexamethonium or hyoscine. Thus the action of potassium chloride is neither nicotinic

nor muscarinic. This agrees with previous reports that the retraction of the cat nicitating membrane obtained on stimulating the superior cervical ganglion with potassium ions is not reduced by ganglion-blocking agents such as tubocurarine (Brown & Feldberg, 1936), tetraethylammonium (Acheson & Pereira, 1946) or hexamethonium (Trendelenburg, 1959), nor by atropine (Brown & Quilliam, 1964b). In contrast, ganglionic depolarization and discharge provoked by barium chloride is antagonized by hexamethonium (Takeshige & Volle, 1964b).

TABLE 1
SUMMARY OF RESULTS

Stimulant drug	Type of ganglionic potential	Effect of blocking agents (D, depression; I, increase; 0, no change)					
		Hexamethonium			Hyoscine		
		Ganglionic potentials −ve	Ganglionic potentials +ve	Post-ganglionic discharge	Ganglionic potentials −ve	Ganglionic potentials +ve	Post-ganglionic discharge
Carbachol	−ve	D	I	D	I	D	D
	−ve/+ve/−ve						
Acetylcholine	−ve	D	I	D	I	D	D
	−ve/+ve/−ve						
Nicotine	−ve	D	I	D	I	D	0
	−ve/+ve/−ve						
Tetramethyl-ammonium	−ve	D	I		I	D	
	−ve/+ve/−ve						
Muscarine	−ve	0		0	D		D
	+ve						
Potassium chloride	−ve	0		0	0		0

Positive ganglionic potentials

All of the drugs in group A were capable of eliciting positive ganglionic potentials. These were not affected by hexamethonium, but were enhanced in the presence of hexamethonium, presumably because the counteracting negative potential was reduced. The positive potentials were all reduced by hyoscine (even those induced by nicotine). The enhancement of the negative potential by hyoscine was probably the result of suppression of a hidden positive potential.

Takeshige *et al.* (1963) and Takeshige & Volle (1964a, b, c and d) have also described positive ganglionic potential changes following injections of acetylcholine and methacholine. Like those reported in the present paper, they were not affected by hexamethonium. Takeshige *et al.* (1963) also reported that the positive potential evoked by methacholine was suppressed by atropine, but that atropine did not affect the positive potential produced by large doses (250 μg) of acetylcholine. Subsequently, Takeshige & Volle (1964d) described a positive potential produced by lower doses (20 μg) of acetylcholine in the presence of hexamethonium which was abolished by atropine. Thus there appears to be some similarity between the positive potentials demonstrated in the present experiments and those reported by Volle and associates.

However, there are also certain important differences. Takeshige & Volle (1964d) found that tetramethylammonium produced only a prolonged negative potential, even after hexamethonium, which was not modified by atropine. In contrast, in the present study the effects of both nicotine and tetramethylammonium appeared to be similar to

those of carbachol: all three drugs could evoke positive potential swings in the presence of hexamethonium, and the positive potentials were reduced, and the negative potentials enhanced, by hyoscine. Secondly, Takeshige and Volle obtained evidence to suggest that the positive potential they detected exerted an inhibitory influence. It was associated either with electrical silence in the postganglionic nerve, or with a reduction of the existent discharge, and also with a reduction of the ganglionic action potentials elicited by preganglionic nerve stimulation. In contrast, the present experiments have shown that the postganglionic nerve discharge elicited by stimulant drugs persisted undiminished during the positive potential phase (Fig. 1), and in some experiments appeared in the absence of any negative potential. Further, when the positive potential was suppressed by hyoscine, the postganglionic nerve discharge was not enhanced, but in some cases was diminished. This positive potential clearly did not exert any considerable inhibitory action.

It is possible to account for positive swings of ganglionic potential of the type described in the present paper in terms of electrotonic spread of ganglionic depolarization along the short postganglionic nerve to the second recording electrode. The postganglionic nerve trunk might then be depolarized at a time when the ganglion cell depolarization had subsided. Burns & Paton (1951) showed that the depolarization of the motor end-plate produced by decamethonium or cathodal current spread a few mm along the muscle fibre membrane. Administration of d-tubocurarine after decamethonium then produced a rapid repolarization at the end-plate but not at the immediately adjacent region, so that the end-plate would be transiently electropositive to the surrounding region. However, in the present study, hexamethonium was administered immediately before, not immediately after, the injection of depolarizing agent. Further, it would be difficult to explain the dramatic effect of hyoscine on the responses to carbachol, and the dissimilarity between carbachol and potassium chloride, on the basis of electrotonic spread of potentials.

It seems more likely that the positive swings of ganglionic potential in the presence of hexamethonium reflect the presence of a ganglionic hyperpolarization, differing from the depolarization in its resistance to hexamethonium and sensitivity to hyoscine. The potential changes normally evoked by stimulant drugs might then be considered the algebraic sum of ganglionic depolarization and hyperpolarization, which fits in with the apparent enhancement of the depolarization by hyoscine.

Effect of hyoscine on postganglionic nerve discharge

Hyoscine abbreviated the postganglionic nerve discharge produced by carbachol, but did not materially affect the discharge elicited by nicotine or potassium chloride. The most reasonable explanation for this would seem to be that the discharge produced by carbachol, particularly the later part of the discharge, is due to a muscarinic type of action. Absence of effect on nicotine or potassium chloride discharge rules out nicotinic or unspecific blocking actions of hyoscine. A partly muscarinic action of carbachol also explains why hexamethonium blocked the discharge produced by nicotine rather more completely than that seen with carbachol. Evidence that the depolarizing action of carbachol involves both muscarinic and nicotinic actions has been described previously (Brown, 1966). Takeshige & Volle (1963) have also described a hexamethonium-insensitive, atropine-sensitive late postganglionic discharge by acetylcholine.

Effect of hyoscine on evoked ganglionic action potentials

Hyoscine did not reduce the spike potential component of the ganglionic action potential recorded in response to synchronous, single preganglionic stimuli. However, it produced a large and prolonged reduction of the after-positivity (P-wave) without affecting the after-negativity. This is similar to the effect of low doses of atropine (Eccles & Libet, 1961; Shand, 1965), and suggests that hyoscine might modify the transmission of high-frequency preganglionic nerve stimulation. It also raises the question of whether there is any fundamental similarity between the ganglionic after-positivity recorded in the response to preganglionic nerve stimulation, and the ganglionic positivity produced by injection of certain stimulant drugs.

SUMMARY

1. Ganglionic potential changes and postganglionic nerve discharges elicited by intra-arterial injection of stimulant drugs to the superior cervical ganglion of anaesthetized cats were recorded.

2. Carbachol, acetylcholine, nicotine and tetramethylammonium evoked either a negative ganglionic potential, or a sequence of negative–positive–negative potential changes, together with a postganglionic nerve discharge. Negative ganglionic potentials and postganglionic discharges were reduced by hexamethonium. Hyoscine elevated the negative ganglionic potential and reduced the positive potential. Hyoscine reduced carbachol or acetylcholine-induced postganglionic nerve discharges, but did not affect those produced by nicotine.

3. Muscarine evoked low-amplitude negative or positive potential changes and a prolonged, low-amplitude discharge. Negative potentials and postganglionic discharge were unaffected by hexamethonium and abolished by hyoscine.

4. Potassium chloride produced a large negative ganglionic potential and a brief postganglionic discharge. Neither were modified by hexamethonium or hyoscine.

5. Hyoscine did not reduce the spike potential or the negative after-potential of the transmitted action potential complex, but strongly reduced the positive after-potential.

6. It is concluded that the stimulant drugs used fall into three classes, and that the ganglionic potentials produced are complex because of the interaction of depolarizing and hyperpolarizing actions.

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