Stellate Ganglionic Transmission and Myocardial Contractile Force during Halothane Anesthesia

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The effect of halothane anesthesia upon transsynaptic transmission in the left stellate ganglion of the dog was determined by simultaneous measurement of postganglionic potentials and the maximal rate of change of myocardial contractile force in response to progressively increasing intensities of preganglionic stimulation. Preganglionic stimulation produced either an increase or the same magnitude of postganglionic potentials and myocardial contractile force response (in percentage) during halothane anesthesia as compared with the control state. These findings are presented as evidence that one mode of stellate ganglionic transmission is unimpaired and even facilitated during halothane anesthesia.

DURING THE COURSE of a series of neurophysiologic studies in our laboratory, we observed that stellate ganglionic transmission was not impaired in the intact dog during halothane anesthesia. It was deemed appropriate to determine the precise relationship between the electrophysiologic activity and the mechanical function of the heart. The technique of eliciting ganglionic responses and recording the evoked action potentials from the postganglionic cardiac fibers was considered a vital part of the design of the study.[1-3] By testing with a large spectrum of graded electrical intensities of stimulation, the evoked graded compound action potentials recorded from postganglionic fibers were measured simultaneously with the changes in myocardial contractile force produced by stimuli of the same intensity.

This study shows that stellate ganglionic transmission is not impaired during halothane anesthesia without the use of cholinergic blocking agents and that the ganglionic and inotropic activities can be dissociated.

Methods

Experiments were performed in 36 mongrel dogs of either sex, weighing from 10 to 20 kg. Each dog served as its own control. Among the 17 successful experiments, five dogs were anesthetized with intravenous chloralose (80 mg./kg.) plus a minimal dose of pentobarbital (5–20 mg./kg.); seven were anesthetized with chloralose alone (80 mg./kg.) and five were anesthetized with pentobarbital (25–35 mg./kg.) only. The basal anesthetics in dosage ranges used in this study had no influence on the ganglionic effects of halothane. Therefore, the results from all three groups were combined for analysis.

The trachea was intubated with a cuffed endotracheal tube after intravenous administration of succinylcholine (20–30 mg.) or gallamine (20–30 mg.). Respiration was controlled by means of a volume-limited respirator with a Frumin valve, using 100 per cent oxygen. Tidal volume and respiratory frequency were kept constant to maintain arterial blood gases within normal limits (pH, 7.36–7.40; P_{CO_2}, 35–42 mm. Hg; P_{O_2}, 200–500 mm. Hg). Arterial blood samples were drawn at regular intervals for measurement of arterial blood gases and halothane concentration. Arterial P_{O_2} was determined with the Clark P_{O_2} electrode (Type E5046) and a Radiometer gas monitor (Model PHA 927 and Model PHM 27, Radiometer, Denmark). Ar-

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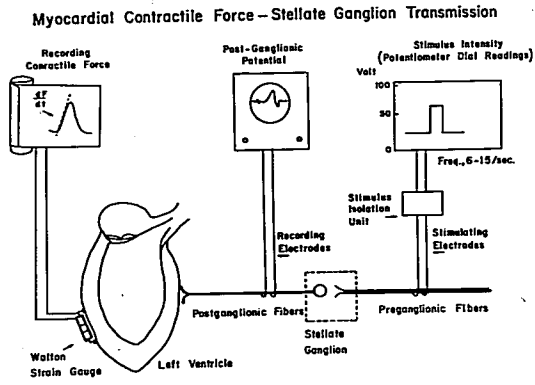

FIG. 1. Diagram of the experimental arrangement. Stimulating electrodes are on the left sympathetic chain level of T1–4 (preganglionic fibers) and recording electrodes on the ventral limb of the ansa subclavia (postganglionic fibers).

terial *p*H and P_{CO_2} were determined with an Astrup microelectrode (Type E5021) and a Severinghaus P_{CO_2} electrode (Type E5036). Halothane was administered via a Model MII Fluotec vaporizer fitted into a non-rebreathing system, starting with an inspiratory concentration of 2.0 per cent for 3–5 minutes, then reduced to 1.0 per cent to maintain a steady state which was assured by periodic determination of arterial halothane concentration. The concentrations of halothane in arterial blood, stellate ganglion and atrial tissue were determined by gas chromatography. In these experiments blood halothane concentration ranged from 8.4 to 29.4 mg./100 ml. (mean 16.6 ± 1.8 mg./100 ml., but the concentration was kept constant during each simultaneous determination of both electrophysiologic and mechanical responses.

A sternal splitting thoracotomy was performed and the left upper three ribs were partially removed at the sternal end. Arterial blood pressure was measured through a short stiff cannula placed into the left femoral artery and connected to a Statham P23Db transducer. Changes in myocardial contractile force were recorded with a Walton-Brodie strain-gauge arch[4] [6] sutured to the surface of the right ventricle. The segment of myocardium beneath the gauge was stretched approximately 50 per cent beyond its initial length. The resultant changes in resistance in the gauge during contraction were amplified using a Wheatstone bridge. Arterial blood pressure and the electrocardiogram were recorded on a multichannel oscillograph (Sanborn, Model 150) at paper speeds of 2 and 100 mm./sec.

Bilateral high cervical vagotomy was performed, and the ventral limb of the ansa subclavia and the left upper thoracic sympathetic chain were exposed by careful dissection. The sympathetic chain was sectioned at the level of T5, including the rami communicantes of T1 to T4. The left sympathetic chain then was placed on the stimulating electrodes (Ag-AgCl) and stimulated electrically using a Grass stimulator (Model S4F) in conjunction with a Grass isolation unit (Model SIU-4B) (fig. 1). Optimal voltage, frequency and duration were determined by the particular experimental objectives. The ventral limb of the ansa subclavia was sectioned near the left inferior cervical ganglion and placed on recording electrodes (Ag-AgCl). The nerve was crushed between the recording electrodes to produce a monophasic response. The left postganglionic responses to electrical stimulation were shown on an oscilloscope (Model 565, Tektronix, Mass.) using a Model 2A61

[6] Evaluation of the dynamic accuracy of the gauge revealed a uniform response (±5 per cent) to 45 cps. with a maximum frequency-phase angle shift of one degree per cycle per sec.[5]

Tektronix preamplifier. Postganglionic responses were photographed using a Polaroid Model-110 camera.

Single square wave pulses from 1 to 5 msec. in duration, of 3–20 volts, which did not cause detectable changes in contractile force, were applied to the sympathetic chain. The postganglionic potential produced by a single stimulus was indicated by the abbreviation PGP_C. After the single stimulus, a train of stimuli (tetanic stimulation) at a constant frequency was applied for 10 seconds using the same intensity as the single shock. The optimal frequency, which was determined at the beginning of each experiment, varied from 6 to 15 cps. Postganglionic potentials produced by the tetanic stimuli were designated PGP_T. Immedaitely after tetanic stimulation another single impulse was applied; the resultant postganglionic potential was identified as PGP_A. Thus, at any given intensity of stimulation the following three sets of potentials were recorded from the ansa subclavia: 1) those obtained by a single stimulus, as controls, PGP_C; 2) those obtained during tetanic stimulation, PGP_T; and 3) those obtained immediately after tetanic stimulation, PGP_A. PGP_A usually showed a variable degree of posttetanic potentiation as previously described by Feng and Li,[6] Larrabee and Bronk,[1] and Standaert.[7] "Graded response curves," *i.e.*, the relationships between either the postganglionic potential or contractile force and the electrical stimuli of graded intensity evoking them, were obtained by measurement of the appropriate parameters corresponding to a particular

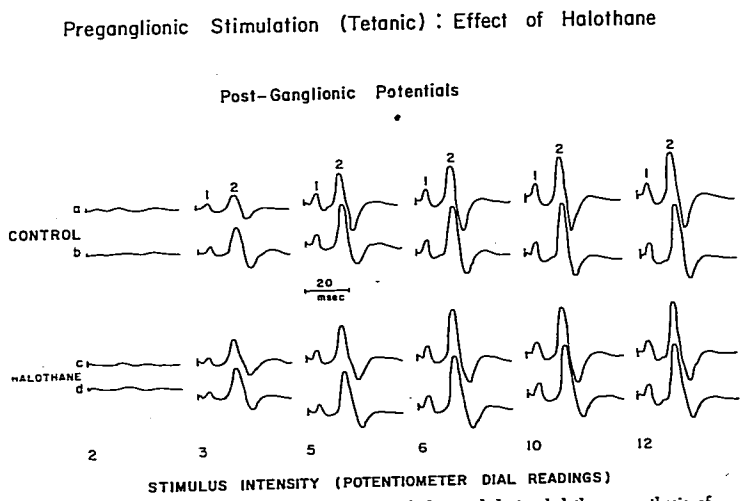

FIG. 2. Evoked postganglionic potential (PGP) before and during halothane anesthesia of a typical experiment. PGP_1: first component, labeled 1; and PGP_2: second component, labeled 2. Postganglionic potentials of increasing height were observed in response to progressively increasing intensities of preganglionic stimuli (see text). Tracings in two upper panels were obtained during control period a) before tetanic stimulation and b) immediately after tetanic stimulation. Tracings in two lower panels were obtained during halothane anesthesia: c) before tetanic stimulation and d) immediately after tetanic stimulation. Magnitude of PGP_1 and PGP_2 is measured from baseline to initial peak. Dip after PGP_2 represents incomplete crushing of the nerve between the two recording electrodes. This does not interfere with the comparison between the control and the anesthetic state.

Observe that the magnitude of the potentials PGP_1 and PGP_2 during halothane anesthesia is equivalent to that obtained during the control state. The myocardial counterpart of these neurophysiologic findings was determined simultaneously and is presented in figure 3.

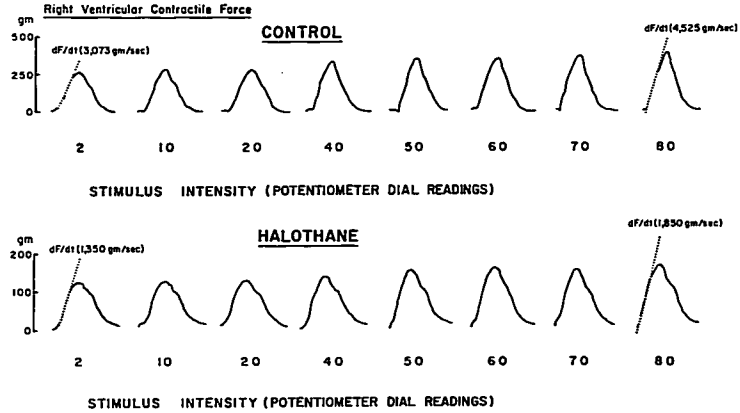

FIG. 3. Maximal myocardial contractile force (F_m) and maximal rate of increase of contractile force (dF/dt) before and during halothane anesthesia. Tracings of Walton-Brodie strain-gauge arch on right ventricle in response to progressively increasing intensities of tetanic stimulation. Paper speed: 100 mm./sec. Note the different calibrations of the ordinate in the upper and lower tracings. Although absolute level of maximal contractile force during halothane anesthesia is significantly lower than during control ($P < 0.01$), the proportional increase due to tetanic stimulation remains the same. Changes in myocardial contractile force were determined simultaneously with the neurophysiologic changes presented in figure 2.

stimulus intensity. For each set of recorded ganglionic potentials there were usually, but not always, two components: the first component was called PGP_1 and the second, PGP_2. PGP_1 probably was the response to stimulation of sympathetic chain B fibers (3–15 m./sec.) and PGP_2 correlated with sympathetic C fibers (<2 m./sec.) (fig. 2).

The maximum rate of change of contractile force (dF/dt) in gm./sec. was calculated from the most rapidly rising segment of the contractile force tracings recorded at a paper speed of 100 mm./sec.[8] (fig. 3). "Peak force" (F_m) also was measured from the high-resolution tracings as the maximal tension developed and indicated by the distance between the baseline and the highest degree of the contraction.[8]

Data for control PGP_C, PGP_T, and PGP_A and series of graded response curves, together with hemodynamic parameters, were obtained before halothane anesthesia, and the procedures repeated during the administration of halothane. In more than half of the experiments, data for the postanesthetic period were obtained as "back" control also, as indicated by determination of the arterial concentration of halothane.

Means, standard deviations, and standard errors of estimate were obtained by Fisher's statistical method.[9] Student's t test was applied. A P value lower than 0.01 was considered significant in this study.

Results

The results consisted of simultaneous measurement of the height of postganglionic potentials (PGP) and changes in myocardial contractile force (as manifested by dF/dt and F_m) produced by tetanic stimulation.

Circulatory Status Before and During Halothane Anesthesia (Without Tetanic Stimulation)

The mean values for heart rate before and during halothane anesthesia were 170 ± 6.3 (SE) and 142 ± 7.1 (SE) beats/minute, respectively; the average decrease in heart rate

TABLE 1. Maximal Responses of Heart Rate and Mean Arterial Blood Pressure (Pma) to Supra-maximal Preganglionic Stimulation Before and During Halothane Anesthesia in 17 Dogs

Expt.	Heart Rate (Beats/min.)				Pma (mm Hg)			
	Before Halo.		During Anesth.		Before Halo.		During Anesth.	
	Before Tet. Stim.	Max. Response %	Before Tet. Stim.	Max. Response %	Before Tet. Stim.	Max. Response %	Before Tet. Stim.	Max. Response %
756	200	+3	164	+15	113	+85	92	+45
676	180	+2	150	+ 1	124	+ 2	82	+12
5176	168	+5	136	+ 9	129	+18	84	+20
536	183	+4	144	+ 1	137	+32	95	+ 5
2106	203	0	201	—	107	+40	40	+73
1186	172	0	124	0	100	+13	64	+ 8
12286	160	—	132	—	122	+12	115	+33
12216	206	0	162	+ 2	132	+30	85	+ 5
695	140	—	118	—	126	—	82	—
5245	140	—	106	—	113	—	65	—
4125	153	—	130	—	143	—	129	—
2105	198	—	160	—	155	—	136	—
1117	114	+5	98	0	110	+32	85	+18
167	142	—	111	—	112	+ 5	80	+ 4
12206	176	+2	180	0	150	+11	147	—
1046	183	0	133	0	131	+19	76	+55
2156	171	+3	141	− 2	106	+13	88	+ 9
Mean	170	+2.2%	141	+2.6%	124	+24.0%	91	+24.0%
S.E.±	6	0.6	6	1.7	4	6.0	6	6.6%
P				>0.5				>0.5

TABLE 2. Maximal Responses in "Peak Myocardial Contractile Force" Tetanic Stimulation Before and During

Expt.	Fm (gm)							
	Before Halothane				During Halothane Anesthesia			
	Before Tetanic Stim.	Maximal Response	Changes in Absolute Values	%	Before Tetanic Stim.	Maximal Response	Changes in Absolute Values	%
676	350	400	+ 50	(+ 14%)	250	288	+38	(+ 15%)
5176	219	544	+325	(+149%)	163	250	+88	(+ 54%)
536	225	350	+125	(+ 56%)	115	155	+40	(+ 35%)
2106	363	425	+ 53	(+ 15%)	259	283	+24	(+ 9%)
1186	144	194	+ 50	(+ 35%)	63	75	+13	(+ 20%)
1117	59	156	+ 97	(+163%)	39	61	+23	(+ 58%)
1046	75	313	+238	(+217%)	56	130	+74	(+137%)
Mean ± S.E.				+93 ± 31%				+47 ± 16% p > 0.2

was 16.4 per cent ±2 per cent ($P < 0.01$) during halothane anesthesia. The average values for mean arterial blood pressure before and during halothane anesthesia were 124 ± 3.8 mm. Hg and 89 ± 6.5 mm. Hg, respectively; during halothane anesthesia the blood pressure decreased an average of 29.9 ± 3.5 per cent ($P < 0.01$).

The average values for maximal contractile force (F_m) decreased from 180 ± 31.2 gm. (the pre-halothane control value) to 112 ± 24.1 gm. during halothane anesthesia; the mean percentage change in F_m was −40 ± 6.3 per cent ($P < 0.01$).

A single preganglionic stimulus (of supramaximal intensity or otherwise) produced no changes in the above values of heart rate, mean arterial blood pressure, and contractile force before or during halothane anesthesia.

Maximal Response to Preganglionic Tetanic Stimulation During Halothane Anesthesia

Heart Rate and Blood Pressure: Table 1 shows the data pertinent to changes in heart rate and mean arterial blood pressure in response to preganglionic tetanic stimulation before and during halothane anesthesia (17 experiments). The maximal percentage changes in heart rate in response to the tetanic stimulation were: during the control state, + 2.2 ± 0.6 per cent, during halothane anesthesia, + 2.6 ± 1.7 per cent ($P > 0.5$). Average maximal responses of mean arterial blood pressure to tetanic stimulation before and during halothane anesthesia were + 24.0 ± 6.0 per cent and + 24.0 ± 6.6 per cent, respectively ($P > 0.5$) (table 1). These findings indicate that there was no significant difference in maximal heart rate and mean arterial blood pressure responses to preganglionic tetanic stimulation before and during halothane anesthesia (table 1).

Contractile Force: Table 2 presents the data pertinent to changes in maximal contractile force (F_m) and the rates of rise of contractile force (dF/dt) in response to tetanic preganglionic stimulation obtained in seven experiments. In all experiments tetanic stimulation caused an increase in F_m both before and during halothane anesthesia. Increments of F_m during the control (pre-halothane) state ranged from 14 to 217 per cent (mean: + 93 ± 31 per cent) and, during halothane anesthesia, from 9 to 137 per cent (mean: + 47 ± 16 per cent) ($P > 0.2$).

The average increase in dF/dt during the control state in response to the tetanic stimulation was 150 ± 68 per cent and during halothane anesthesia 104 ± 49 per cent. The

(F_m) and "Rate of Rise of Contractile Force" (dF/dt) to Supra-maximal Halothane Anesthesia in Seven Dogs

dF/dt (Kg/sec)							
Before Halothane				During Halothane Anesthesia			
Before Tetanic Stim.	Maximal Response	Changes in Absolute Values	%	Before Tetanic Stim.	Maximal Response	Changes in Absolute Values	%
6196	8889	+2693	(+ 43%)	4038	5750	+1712	(+ 42%)
5500	1308	+7582	(+138%)	2015	3433	+1418	(+ 70%)
3096	4648	+1552	(+ 50%)	1500	2237	+ 737	(+ 49%)
4896	5573	+ 677	(+ 14%)	3846	4271	+ 425	(+ 11%)
1604	2642	+1038	(+ 65%)	1444	2222	+ 778	(+ 54%)
1124	3919	+2795	(+249%)	533	1083	+ 572	(+112%)
1206	7133	+5927	(+491%)	661	3250	+2489	(+392%)
		+150 ± 68%					+104 ± 49% p > 0.5

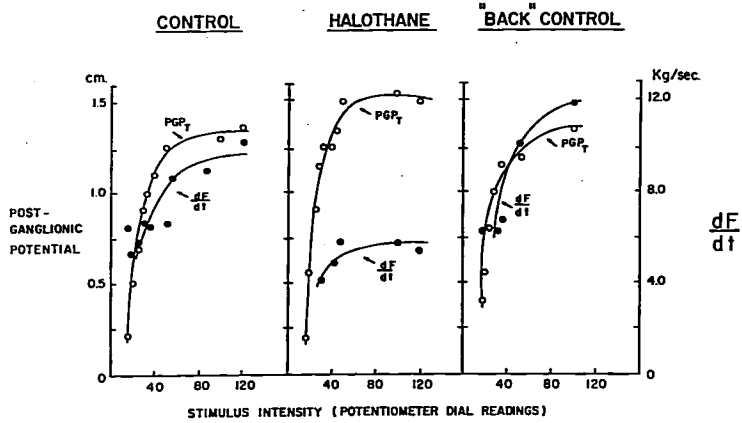

FIG. 4. "Graded response curves" of evoked postganglionic potentials (PGP's) obtained by plotting magnitudes against increasing intensities of the preganglionic tetanic stimulus, before, during and after halothane anesthesia. Simultaneously determined dF/dt values were calculated (see text). dF/dt values also increased progressively with increasing intensities of stimulation, forming "graded response curves." Note the striking difference in the levels of the two types of "graded response curves": PGP_T (during tetanic stimulation) curves are elevated during halothane anesthesia, in contrast to the severe drop of the dF/dt curve.

mean increase in dF/dt during halothane anesthesia was not statistically different from that obtained during the control state ($P > 0.5$) (table 2).

"Graded Response Curves" Before and During Halothane Anesthesia (Produced by Tetanic Stimulation in Increasing Intensities

Single shocks delivered to the sympathetic chain resulted in a postganglionic potential, but there was no change in any hemodynamic parameter. When the sympathetic chain was stimulated tetanically (6–15/sec.) and postganglionic potentials (PGP) were observed, their heights increased with the increasing intensity of stimuli (fig. 2). In addition, there was an increase in the rate of development of myocardial contractile force and peak force (*i.e.*, dF/dt and F_m). The degrees of increase in dF/dt and F_m also varied according to size of preganglionic tetanic stimulus (fig. 3). Two types of "graded response curves" were produced, therefore: one for PGP (figs. 2, 4, 5 and 6) and the other for F_m and dF/dt (figs. 3 and 4).

Postganglionic potentials (PGP), whether resulting from single-shock stimulation (one every 5–20 sec.) or tetanic stimulation (6–15/sec.), showed progressive increases in heights of potentials as the intensity of the stimulus increased (fig. 2). The intensity of the stimulus at which the response began to saturate (*i.e.* did not increase further) varied with each preparation, but throughout any one experiment the stimulus intensities required to produce threshold, submaximal, maximal and supramaximal responses were the same for all series of measurements before, during and after halothane anesthesia.

During halothane anesthesia (blood concentration 8–25 mg./100 ml.) preganglionic tetanic stimulation consistently produced an increase in mean arterial blood pressure and in myocardial contractile force (F_m and dF/dt), although the increase started from a lower base-line (tables 1 and 2). There was no significant difference in the maximal responses

during halothane anesthesia as compared with the control (pre-halothane) period. More striking was the unimpaired transmission through the stellate ganglion, as shown in figures 2, 4, and 5.

Figure 2 shows the responses to stepwise increases in the intensity of preganglionic stimulation as manifested by the heights of postganglionic potentials (PGP). A plateau was reached at the same stimulus strength during halothane anesthesia as in the control (pre-halothane) period. Recordings of postganglionic potentials revealed no depression attributable to halothane (fig. 2).

Figures 4 and 5 show the results of two typical experiments using "graded response curves". In figure 4, the curves for both dF/dt and postganglionic potentials in the control, halothane and "back" control period are superimposed. It is obvious that the curves for dF/dt were reduced markedly to a lower level, but the postganglionic potential (PGP) curves were all well maintained at either the pre-halothane or the "back" control level. In contrast to PGP_C and PGP_A curves, the PGP_T curves (representing evoked-potential during tetanic stimulation) were raised to higher levels during halothane anesthesia as shown in both figure 4 and figure 5. Simultaneous determinations of the PGP_T and PGP_C curves revealed the expected usual lowering of the PGP_T curves in the pre-halothane period (fig. 6) but during halothane anesthesia this situation was reversed, that is, the PGP_T curve became higher (fig. 5). More interesting was the fact that these

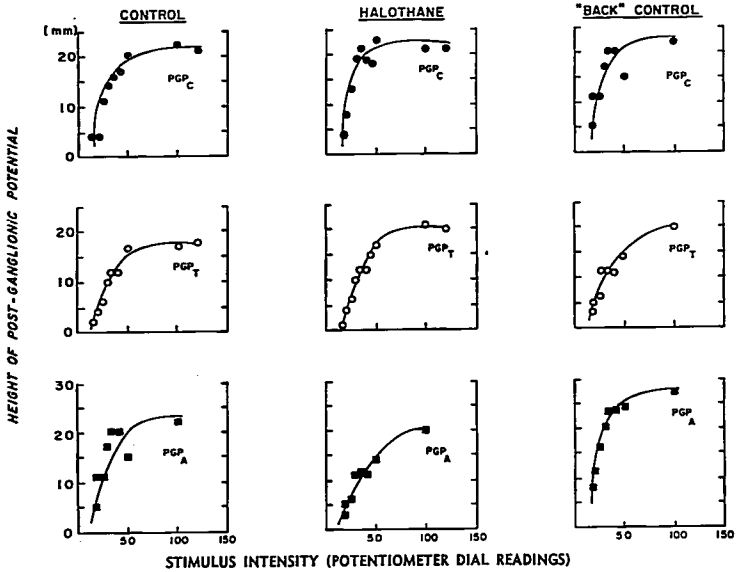

FIG. 5. "Graded response curves" of evoked postganglionic potentials (PGP's) obtained by plotting magnitude of PGP against increasing intensity of preganglionic tetanic stimulation before, during and after halothane anesthesia. Three series of curves are shown from a typical experiment. PGP_C, PGP_T, and PGP_A are the postganglionic potentials obtained before (C), during (T) and after (A) tetanic stimulation, respectively.

Note the similarity in responses including the PGP_T curves which were higher during halothane than in the control and "back" control states.

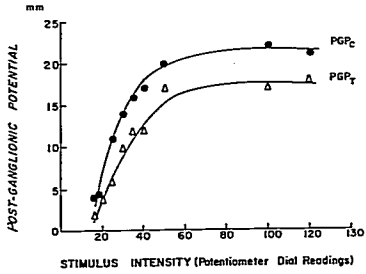

FIG. 6. Two postganglionic potential "graded response curves" superimposed to show the reduced height of PGP_T as compared with PGP_C during the control state before halothane anesthesia. PGP_C: postganglionic potentials obtained before tetanic stimulation: upper curve. PGP_T: postganglionic potentials obtained during tetanic stimulation: lower curve.

curves were obtained from the same experiment. It is clear, therefore, that the electrophysiologic response was unaffected by halothane (arterial concentration in the range of 8–25 mg./100 ml.) (figs. 5 and 6), whereas simultaneously recorded myocardial contractile force (table 2, fig. 4) was depressed severely.

CONFIRMATIVE CONTROL EXPERIMENTS:

Effects of Basal Anesthetics. In the 17 experiments, five of the dogs were anesthetized mainly by chloralose plus small amounts of pentobarbital, seven were anesthetized by chloralose alone, and the remaining five by pentobarbital alone. The results show that the effects of clinical levels of halothane anesthesia on stellate ganglionic synaptic transmission as well as on myocardial response were not significantly different in the three groups of experiments, and all yielded similar patterns of responses.

Affirmation of Halothane Concentration in Stellate Ganglion. To ascertain the concentration of halothane in the stellate ganglion, the ganglionic tissue was dissected in part or *in toto* for analyses in four experiments. The values were 66, 41, 62 and 192 mg. per gm. tissue (wet weight).

Possibility of Some Preganglionic Fibers Passing through the Stellate Ganglion without Synapses. The possibility that some preganglionic fibers did not synapse in the stellate ganglion before forming the ansa subclavia was ruled out by three experiments in which antidromic stimulation of the ventral or the dorsal limb of the ansa subclavia was carried out and no potentials were recorded from the sympathetic chain. Nerve impulses were not conducted through the ganglion antidromically.

Maintenance of Blood Gases at Physiologic Levels. Mean values of arterial blood, *p*H, P_{CO_2} and P_{O_2}, before, during and after halothane anesthesia (table 3) showed that the blood gases were maintained within physiologic limits throughout the experiments.

Discussion

This study demonstrates that stellate ganglionic transmission is unimpaired during surgical levels of halothane anesthesia because ganglionic transmission, directly measured, was unchanged during halothane anesthesia which depressed a phase of myocardial performance as measured by the highest rate of change of the myocardial contractile force (dF/dt), and the maximal magnitude of contraction (F_m).

The preparation was such that neural activity resulting from preganglionic stimulation reached the heart only through the stellate ganglion. The sympathetic chain was severed at T5 and the rami from T1 to T5 also were sectioned. As confirmation for this, cocaine was applied to the stellate ganglion; this completely eliminated postganglionic neural and myocardial responses to preganglionic stimulation, suggesting that the only route for nerve impulses was through the stellate ganglion. The possibility of transmission without synapse in the stellate ganglion was eliminated by showing that stimulation of the postganglionic nerve produced no presynaptic response: synaptic transmission, unlike axonal conduction, is unidirectional. Furthermore, the postganglionic potentials during tetanic stimulation (6–15/sec.) always were reduced, compared with single stimulation at a rate of 2–10/sec., indicating the presence of a synapse (see fig. 6, comparing PGP_C to PGP_T). It was unlikely that the stimulating current could spread far enough to stimulate postganglionic fibers directly because the distance between the stimulating electrodes and the stellate ganglion was

usually about 40 mm. In addition, the latency of the first wave of the postganglionic potential (PGP_1) was about 4 msec. (fig. 2), much longer than the latency of 1 msec. or less than one would expect with direct postganglionic stimulation.

Chemical analysis of extirpated ganglia revealed that the halothane in fact was reaching the ganglion. Furthermore, when the concentration of halothane was increased beyond surgical levels (arterial concentration 40 mg./100 ml.), the postganglionic potential decreased. This, however, merely indicated that halothane could depress ganglionic transmission but only upon overdosage. Still, a concentration of halothane of 10–25 mg./100 ml. in arterial blood produced no ganglionic depression, while at the same time myocardial contractile force was depressed severely.

When halothane was administered there was a significant depression in heart rate, mean arterial blood pressure and myocardial parameters such as F_m and dF/dt. Preganglionic stimulation still produced an increase in the myocardial contractile force; however, it was generally less than in the control state. This could not have resulted from depression of transmission through the stellate ganglion because the postganglionic potentials, directly recorded, showed no change in absolute height and in the PGP "graded response curves."

In order to understand the difference between our findings and those of others,[10, 11, 12, 13, 14] it is pertinent first to review reports that suggest that halothane causes ganglionic blockade. Raventos found that halothane depressed transmission through the superior cervical ganglion of the decerebrated cat, as evidenced by a decreased response of the nictitating membrane to preganglionic stimulation.[10] However, he did not distinguish between the effects of halothane on the nictitating membrane and on the ganglion. Purchase[12] concluded that halothane depressed ganglionic transmission, based upon the depression of the pressor response during halothane anesthesia. However, other anatomical structures involved in the pressor response (besides the stellate ganglion) might have been depressed by halothane. Price *et al.*[13] compared the response (of heart rate) to preganglionic and postganglionic stimulation before and after halothane anesthesia, and concluded that there was depression of ganglionic transmission since the response to preganglionic stimulation was more depressed by halothane than the response to postganglionic stimulation. Their methods, however, were not specific and they could only estimate the degree of blockade. Furthermore, if the heart were affected by halothane it could not summate the widespread effects of preganglionic stimulation, as compared with the lesser effects of postganglionic stimulation affecting a smaller area of the heart.

It has been generally accepted that the amplitude of the postganglionic compound action potential is a measure of the number of ganglion cells responding to the preganglionic stimulation.[1, 2, 3] As the intensity of the stimulus increases, a greater population of ganglionic cells is excited and this progressive increase in the number of responding ganglionic cells is detected as an increase in height of the postganglionic potential. The several components of the postganglionic potential represent the discharge from stimulation of two groups of preganglionic fibers corresponding to B and C fibers, respectively. In the present study each component (PGP_1 and PGP_2) was measured separately. Neither component of the postganglionic potential (PGP_1 and PGP_2) showed any significant change in magnitude during halothane anesthesia, as compared with the control state and in response to tetanic stimulation ($P > 0.4$ and $P > 0.5$).

TABLE 3. Average Values of arterial *p*H, $Paco_2$ and Halothane Concentration in 17 Experiments

	Control (Mean ± SE)	Halothane Anesthesia (Mean ± SE)
*p*H	7.37 ± 0.01	7.39 ± 0.01 ($p > 0.5$)
pco_2 (mm. Hg)	36 ± 1.7	34 ± 1.6 ($p > 0.3$)
po_2 (mm. Hg)	338 ± 42	387 ± 45 ($p > 0.1$)
Halothane concentration (mg./100 ml.)	0	16.6 ± 1.8

Other investigators[15,16] have administered atropine as a muscarinic blocker and have shown that halothane can produce stellate ganglionic blockade, using change in heart rate as an indicator. Eccles,[17] Eccles and Libet,[18] Takeshige and Volle[19] and Volle[20] have shown that the pharmacology of the stellate ganglion is complicated, involving at least three types of ganglionic transmission related to muscarinic, nicotinic and adrenergic effects. In our preparation, myocardial contractile force and the postganglionic potentials were used as indicators, and atropine was not used, so that the situation was not equivalent to those of the other investigations.

There were no significant changes in heart rate when preganglionic fibers of the left stellate ganglion were stimulated, either before or during halothane anesthesia (table 1). The lack of chronotropic response was probably the result of stimulation of the left stellate ganglion instead of the right. It has been shown that stimulation of the left stellate ganglion in the dog results in a positive inotropic effect with minimal chronotropic effects. In contrast, stimulation of the right stellate ganglion results in an increase in heart rate and minimal change in contractility.[21,22]

The strain-gauge arch was used in this study to evaluate one facet of the myocardial performance. By determining the maximum height of contraction (F_m) and the maximum rate of change in contractile force (dF/dt) information was obtained relating to the force generated in the ventricle during the isometric phase of systole. The reduction in F_m and dF/dt has been ascribed to the influence of halothane upon the contractile element of myocardium.[23] Aygen and Braunwald have established the validity of the strain-gauge arch in the assessment of myocardial performance in the intact heart.[8]

The observed depression of contractile force in the presence of unimpaired stellate ganglionic transmission during halothane anesthesia is offered as evidence of a dissociation of the effects of halothane anesthesia upon myocardial and ganglionic function.

Summary

Stellate ganglionic transsynaptic transmission was studied by stimulation of preganglionic fibers and recording of postganglionic potentials in the intact dog before and during halothane anesthesia. The electrophysiologic responses to graded increases in the intensity of the stimulus were compared with the myocardial mechanical responses (ventricular contractile force: F_m and dF/dt).

The intensity of the stimulus at which the response approached saturation varied with each preparation, but in any one experiment the stimulus intensity required to produce threshold and supramaximal responses was the same for all series of measurements before, during and after halothane anesthesia. In every instance the graded response curves of the postganglionic potentials showed no depression during halothane anesthesia. This constitutes the evidence that one mode of stellate ganglionic transmission is not impaired during halothane anesthesia.

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Anesthesia

PREMATURE LABOR Several investigators have noted that as little as 100 mg. of meperidine given during labor will affect the fetus, as shown by lowering of Apgar scores, need for resuscitation or reduction of minute volume. Presumably, this would be even more true in the premature. In a controlled double-blind study of 1,002 premature infants whose mother received either meperidine 100 mg., meperidine 100 mg. and scopolamine 0.4 mg., scopolamine 0.4 mg., or saline intramuscularly during labor, infants were considered to be born of an "uncomplicated" pregnancy if prematurity was the only aberration. If other complications, such as maternal hypertension, anemia, diabetes, sensitization, bleeding, etc., were involved the infant was placed in the "complicated" group. Low spinal anesthesia was commonly utilized for delivery. Regardless of whether the labor and pregnancy had been complicated, when the mother received 100 mg. of meperidine during labor, there was no clinical effect on death rates, incidence of respiratory distress, Apgar scores, need for resuscitation, or incidence of severe neurologic defects within one year. (*Kaltreider, D. F.: Premature Labor and Meperidine Analgesia, Amer. J. Obstet. Gynec. 99: 989 (Dec.) 1967.*)

ABSTRACTOR'S NOTE: Because this publication is at variance with results of earlier work, we must await further investigations to ascertain its validity. Determination of infant blood gases and acid-base status in the first few hours of life would be helpful in this regard.