maintained during the after-potential and outlasts the after-potential at the same depolarizing level if the pulse duration is prolonged beyond the end of the after-potential. The spike of the action potential is not modified by the middle-frequency current flow, but deformation of the late falling phase appears. The negative after-potential cannot appear because of the formation of a plateau, and final repolarization is postponed to the end of the middle-frequency pulse.

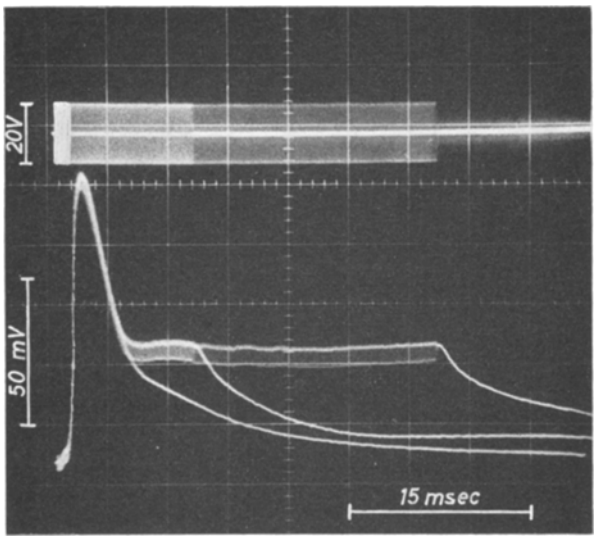


Fig. 2. Effect of prolongation of middle-frequency pulses beyond utilization time on the shape of the transmembrane potential change. Three responses of the same fibre to pulse durations of 1, 10 and 30 msec at same voltage (upper beam with scale on the left) recorded as transmembrane potential (lower beam with scale on the left). Note that compared with 1 msec response (utilization time) the pulses of 10 and 30 msec duration cause a maintained depolarization after the spike, without deforming the latter and postpone the final repolarization to the end of the middle-frequency pulse.

Further experiments demonstrated the local nature of the initial depolarization which occurs during the utilization time of middle-frequency pulses (see Figure 1). This was shown by comparing the shape of the action potential recorded at the site of stimulation with that obtained on the same fibre stimulated at a distance of 25 mm from the site of recording. In experiments to be reported in detail in a later paper, it was also shown that application of middle-frequency pulses to muscle immersed in sodium-free Ringer's solution, no longer produced local depolarization, and hence no action potential. This may suggest that middle-frequency stimulation causes primarily an increase of the sodium permeability of the membrane that consequently leads to an increase in sodium influx across the cell membrane.

*Zusammenfassung.* Der Froschsartorius wird mit Mittelfrequenz(20 kHz)-Stromstössen quer gereizt. Die Reizantwort wird mit intracellulärer Mikroelektrode am Reizort abgeleitet. Die lokale Depolarisierung und die daraus sich ergebende Auslösung des Aktionspotentials werden auf ihre Abhängigkeit von Stärke und Dauer der Reizimpulse untersucht.

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## Effects of Angiotensin on the Superior Cervical Ganglion of the Cat

HAEFELY et al.[1] have recently reported that very low doses of bradykinin and angiotensin produce an inhibition of synaptic transmission in the superior cervical ganglion of the cat.

In this paper, we wish to report a dose-effect relationship obtained with minute quantities of angiotensin on the same preparation.

*Material and methods.* The effects of preganglionic cervical sympathetic nerve stimulation were estimated either by recording nictitating membrane contraction with an isotonic myograph transducer or by the oscilloscopic measurement of the amplified postganglionic nerve action potentials. Close retrograde intra-arterial injections were made towards the superior cervical ganglion through a polyethylene cannula inserted into the ipsilateral lingual artery.

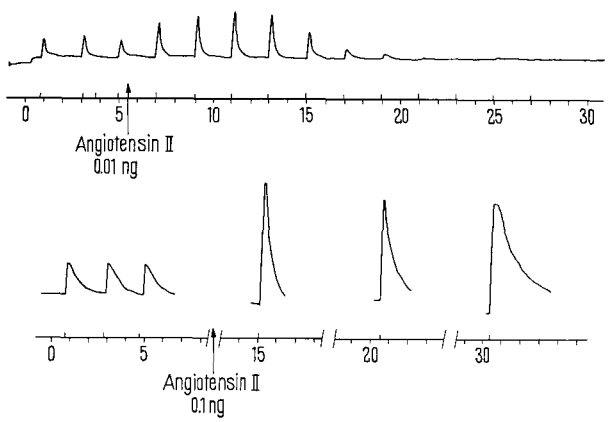
*Results and discussion.* When angiotensin was injected towards the ganglion in amounts too small to contract directly the nictitating membrane (0.5–10 ng), contraction of the ipsilateral membrane was nevertheless elicited. Section of the postganglionic trunk or extirpation of the ganglion abolished this contraction, whereas it was not prevented by bilateral adrenalectomy. Hexamethonium (0.1–1 mg) as well as atropine (100–200 $\mu$g) effectively blocked membrane contraction induced by angiotensin (0.5–10 ng) or by preganglionic stimulation. However, hexamethonium, in similar amounts, failed to abolish the contractions obtained when higher doses of the hormone were applied to the ganglion (0.1–1 $\mu$g), as previously observed by LEWIS and REIT[2].

In addition to stimulating the postganglionic fibres, angiotensin may alter ganglionic transmission when injected towards the ganglion at a concentration insufficient to elicit membrane contraction. In the course of stimulating the preganglionic nerve with submaximal shocks (0.1 sec square waves at a frequency of 15–25 c/sec during 5 sec every 2 min), a retrograde injection of angiotensin (0.01–0.1 ng) resulted in a one- to fourfold enhancement of the response to subsequent stimulations. The response was evaluated by measuring nictitating membrane contractions or by recording postganglionic action potentials. In some preparations, this potentiation of synaptic transmission lasted for 3 h or more (lower tracing, Figure).

[1] W. HAEFELY, A. HÜRLIMANN, and H. THOENEN, Biochem. Pharmac. *14*, 1393 (1965).

[2] G. P. LEWIS and E. REIT, J. Physiol. *179*, 538 (1965).

Very low doses of angiotensin had an opposite effect since 0.0001–0.01 ng of the hormone inhibited contractions induced by preganglionic stimulation (upper tracing, Figure). This inhibitory effect was prevented by dihydroergotamine (500 $\mu$g to 1 mg), a finding which could implicate norepinephrine in the synaptic effects of angiotensin.




Effect of angiotensin on transmission in the cat superior cervical ganglion. Contractions of the nictitating membrane induced by submaximal preganglionic stimulation applied for 5 sec every 2 min at a rate of 15 c/sec. Upper tracing: injection of 0.01 ng of angiotensin. Lower tracing: injection of 0.1 ng of angiotensin. Time marker: 1 min.

The effect of angiotensin on ganglionic transmission therefore appears to be dose-dependent, a phenomenon also noted by HAEFELY et al.[1]. The idea that angiotensin modifies synaptic transmission by facilitating the release of acetylcholine at the preganglionic nerve endings is compatible with these results[3].

*Résumé.* En quantités inférieures à 10 picogrammes, l'angiotensine inhibe la transmission synaptique du ganglion cervical supérieur du chat, et cet effet est antagonisé par la dihydroergotamine. En quantités supérieures à 10 picogrammes, l'angiotensine facilite la transmission synaptique, et de plus, stimule directement les cellules ganglionnaires.

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*February 18, 1966.*

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## Testicular Degeneration in Rats by Carbon Tetrachloride Intoxication

Induction of hepatic lesion[1] and hepatogenic diabetes[2], activation of sympathetic nervous system[3] along with an increased release of catechol amines from adrenal medulla[4], and adrenal cortical hypertrophy and hyperfunction[5] by carbon tetrachloride have previously been described. Gonadal inhibition has been noted in rats after stressful stimuli – such as injection of alloxan, thyroxine, reserpine, chlorpromazine, 10% neutral formalin and epinephrine or norepinephrine. The present experiment has therefore been devised to see whether carbon tetrachloride has any interfering action in the testicular physiology of rats.

Twelve adult rats were selected for the experiments. Six of them received 0.3 ml/100 g carbon tetrachloride and coconut oil mixture (1:1) by the intraperitoneal route. The remaining six similarly received only coconut oil of an equal amount. Both the groups of animals were allowed to eat and drink ad libitum. On the 15th day of the experiment, animals of the experimental ($CCl_4$-treated) and control (oil-treated) groups were sacrificed. The testes, seminal vesicles and the pituitary of the animals were excised and immediately weighed on a torsion

[1] V. A. DRILL, Pharmac. Rev. *4*, 1 (1952).
[2] C. M. LEEVY, C. M. RYAN, and J. C. FINBERG, Am. J. Med. *8*, 290 (1950).
[3] D. N. CALVERT and T. M. BRODY, Am. J. Physiol. *198*, 669 (1960).
[4] T. M. BRODY and D. N. CALVERT, Am. J. Physiol. *198*, 682 (1960).
[5] A. CHATTERJEE and N. R. BARDHAN (to be published) (1965).

Effect of $CCl_4$ on testes, seminal vesicle and pituitary weights in rats

| Group | No. of rats | Body weight (g) | Weight of testes | | Weight of seminal vesicles | | Weight of Pituitary | |
|---|---|---|---|---|---|---|---|---|
| | | | Actual (g) | Relative (g/100 g) | Actual (mg) | Relative (mg/100 g) | Actual (mg) | Relative (mg/100 g) |
| Control | 6 | 153 ± 5.12[a] | 2.36 ± 0.11[a] | 1.55 ± 0.04[a] | 472 ± 15.42[a] | 309.5 ± 5.90[a] | 5.0 ± 0.25[a] | 3.23 ± 0.09[a] |
| Experimental ($CCl_4$-treated) | 6 | 150 ± 6.83 | 1.48 ± 0.21 | 0.98 ± 0.12 | 191 ± 28.60 | 127.2 ± 17.11 | 7.3 ± 0.42 | 5.0 ± 0.14 |

[a] Means S.E.M.