The Axon Reflex Sweating Produced by Potassium and Sodium Cyanides

In human skin, sweating is produced through axon reflex mechanism by intradermal injection of nicotine and other agents with nicotinic action[1], and also by sodium chloride and some other sodium salts[2]. The axon reflex sweating can be elicited also in the toe-pads of the cat by nicotine and sodium chloride: this response is abolished by degeneration of the postganglionic sympathetic nerves, but not influenced by degeneration of the sensory nerves supplying the toe-pads[3]. The receptors responsible for this sweating are presumed, for the present, to be specialized parts of the sympathetic sweat nerve endings.

In the present experiments, we investigated the effect of potassium and sodium cyanides on the receptors for the axon reflex sweating and found that the cyanides themselves have a property of provoking the axon reflex response by acting on the receptors.

Observations were made on the toe-pads of nine cats of both sexes, weighing 2·2 to 3·6 kg. The techniques used were the same as those described in our previous paper[3]. In order to exclude sweating of central origin in the toe-pads of the hind feet, the sciatic nerves were sectioned about 4 to 5 h previously under ether anaesthesia. To visualize sweating, the iodine-starch method of WADA and TAKAGAKI[4] was used. For identification of the axon reflex sweating, the band method[2] was applied. The test agents used were dissolved in 0·9% NaCl solution and injected subcutaneously to the toe-pads on the distal side of the band under non-anaesthesia, as illustrated in the Figure.

The effect of KCN on the axon reflex sweat response to nicotine was studied in 4 cats. Injection of 0·05 ml of nicotine in 10^{-4} or 10^{-3} on the first day after section of the sciatic nerves showed an evident axon reflex sweating in all of toe-pads tested. As described in a previous paper[3], the responsiveness of each toe-pad to the axon reflex provoking action of nicotine diminished more or less rapidly, as the days elapsed. On the 5th to 7th day after the sciatic nerve section, the response became doubtful or no longer detectable even with 10^{-2} nicotine.

In most experiments, KCN in 10^{-3} was applied in mixture with nicotine in 10^{-4} to 10^{-2}. No evidence was obtained to indicate that KCN inhibits the axon reflex response to nicotine. Injection of KCN in 10^{-3} alone elicited occasionally a slight sweating around the site of injection. KCN in 10^{-2} alone was tested in the fourth cat on the second day after the nerve operation. It was an unexpected finding that this concentration of KCN produced a vigorous axon reflex sweating.

In 18 out of 23 tests in 6 cats, performed on the first to third day after the sciatic nerve section, the axon reflex sweat response was observed with KCN in 10^{-2}. The failure of the response in 5 tests was proved to be due to the decreased sensitivity of the receptors for the axon reflex. The response commenced usually within 20 to 50 s after the start of injection. Not rarely, over 100 sweat spots were counted on either side of the band. The pattern of the response was quite analogous to that of the axon reflex sweating produced by nicotine. Then, attempts were made to determine the effects on the sweat response to KCN of procaine hydrochloride, atropine sulphate and hexamethonium bromide.

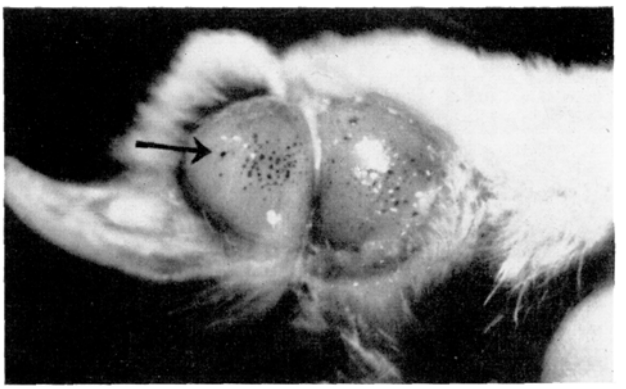

Fig. 1. – The axon reflex sweating on the cat's toe-pad. A band was applied across the middle part of the toe-pad on the second day after section of the sciatic nerve. Subcutaneous injection of 0·05 ml of 10^{-2} KCN (in mixture with hexamethonium) was made to the distal side of the band. Sweating was visualized as black spots. The site of injection is indicated by arrow. White spots on the toe-pad are caused by reflection of light. Magnification, 3·5 ×.

The effect of procaine in 10^{-3} was examined in 13 tests in 5 cats: in all tests the sweat response to KCN in 10^{-2} was completely inhibited. Likewise, the effect of KCN was abolished by atropine in 10^{-3} in all of 12 tests in 4 cats. On the contrary, hexamethonium in 10^{-3} was without any inhibitory effect in all of 22 tests in 5 cats (Figure). These results are very similar to those obtained from the experiments on the axon reflex sweating produced by high concentration of NaCl[5]. This fact supports the view that the axon reflex sweating occurs without synaptic transmission by acetylcholine as in the sympathetic ganglion. The failure to see the axon reflex response after injection of KCN in mixture with procaine or with atropine could not be attributed to the decreased sensitivity of the receptors, since positive results were obtained in most of the tests in which the same concentration of KCN was applied alone or in mixture with hexamethonium to the same toe-pads the following day.

In addition, the effect of NaCN was studied in two cats: injection of NaCN in 10^{-2} also provoked a definite axon reflex sweating. Injection of NaCN in 10^{-3} produced a doubtful response, but a subsequent injection of NaCN in 10^{-2} was fully effective.

Further, the axon reflex nature of the sweating produced by the cyanides was confirmed by observations on human skin, using the band method[2]. Intradermal injections of 0·1 ml of NaCN in 10^{-3} and 10^{-2} were made to the dorsal surface of the forearms of one of us (K.). With NaCN in 10^{-2}, the sweat spots began to appear around the wheal of injection within 40 s after the start of injection and spread very rapidly and widely to the uninjected side beyond the band. The size of the sweating areas reached its maximum, e.g. 37 cm², within 6 min after injection. NaCN in 10^{-3} was also effective, but the extent of the response produced was much smaller.

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The receptors for the axon reflex sweating have a property of being stimulated by nicotine and agents with nicotinic action, in common with the sympathetic ganglion cells and the carotid body chemoreceptors. The similarities and differences between the properties of the latter two structures were comprehensively reviewed by KONZETT and ROTHLIN[6]. The sympathetic ganglion cells have been shown to be selectively paralyzed by the cyanides[7]. Since the work of HEYMANS *et al.*[8], the cyanides, on the other hand, have been known to stimulate the carotid body chemoreceptors. In this respect, the receptors responsible for the axon reflex sweating resemble the carotid body chemoreceptors.

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Zusammenfassung

Subkutane Einspritzung von Kalium- oder Natriumzyanid in die Zehenballen der Katze führt über einen Axonreflex zu merklichem Schwitzen. Dieser Effekt von Kaliumzyanid wird durch Procain und Atropin gehemmt, nicht aber durch Hexamethonium. Auch beim Menschen ruft intrakutan eingeführtes Natriumzyanid eine entsprechende Schweissabsonderung hervor.

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The Influence of Frequency of Stimulation on Synaptic Transmission at Different Temperatures

Cooling of the ganglion causes failure of the nictitating membrane contractions on preganglionic nerve stimulation[1]. In some of our preliminary experiments[2], we noticed that at higher frequencies of stimulation nictitating membrane contractions failed earlier on cooling the ganglion. In this communication we report some further experimental results concerning this effect of different frequencies. In some experiments nictitating membrane contractions were recorded, in others the acetylcholine output was determined.

The superior cervical ganglion of chloralosed cats was perfused in the usual way. The cervical sympathetic trunk was stimulated with square voltage pulses of 1 ms duration at frequencies of 2, 10 and 15 shocks per s. The ganglion was heated or cooled in the way described in one of our earlier papers[3]. The temperature was measured by means of a thermocouple connected to a galvanometer. Nictitating membrane contractions were recorded with an isotonic lever. In experiments in which the acetylcholine output was determined, the post-ganglionic trunk was tied and eserine sulphate (1:100000) added to Locke's solution. Acetylcholine was assayed on blood pressure of eviscerated chloralosed cats.

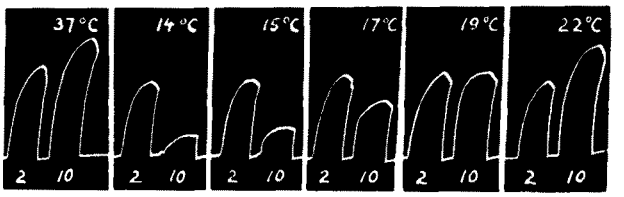

Fig. 1. – Cat, chloralose. Nictitating membrane contractions at different temperatures in the range from 14°C to 37°C. Preganglionic nerve stimulation at 2 and 10 shocks per s.

Figure 1 shows the response of the nictitating membrane to preganglionic stimulation at 2 and 10 shocks per s at 37°C. At 14°C the response of the membrane was considerably more affected for higher rates of stimulation. By increasing the temperature the response to high frequencies gradually returned to its normal value. At temperatures recorded in this experiment (14°, 15°, 17°, 19° and 22°C), the response of the membrane to low frequency stimulation was practically unaffected by temperature changes. These results are in good agreement with those reported by DOUGLAS and MALCOLM[4], who found that an inhibition to high frequency of stimulation preceeded the cold block in cat nerves.

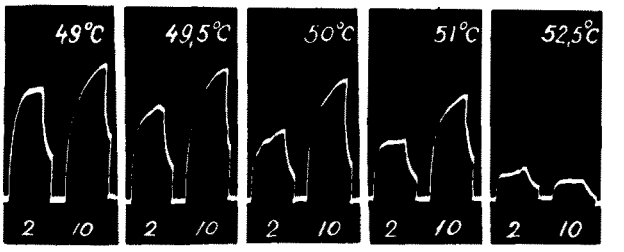

Fig. 2. – Cat, chloralose. Nictitating membrane contractions at different temperatures in the range from 49°C to 52,5°C. Preganglionic nerve stimulation at 2 and 10 shocks per s.

At high temperatures opposite effects were observed. High frequencies of stimulation were more effective. Gradual failure of the membrane contractions to low frequency stimulation started at 49·5°C (Fig. 2). The response to high frequency stimulation was almost unimpaired up to 50·8°C when a steep fall began. At 52·5° C the response to both frequencies was much reduced.

Figure 3 summarises our results. The response of the membrane (on logarithmic scale) has been plotted against the temperature. Two different curves were thus obtained, one for the low frequency (2/s, black dots), the other (circles) for the high frequency of stimulation (10/s). The low frequency curve is shifted to the left in the whole range of temperatures recorded in these experiments.

The influence of frequency of stimulation was also noticable in experiments in which the acetylcholine output was determined at different frequencies. Figure 4 shows the result of four experiments performed at 37°C and at 20°C, respectively. At 37°C the output of acetyl-

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