CHLOROFORM AND REVERSAL OF REFLEX EFFECT.

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In his work on reflex factors influencing arterial blood-pressure Bayliss[1] has shown that in the rabbit the reflex effect of stimulating afferent nerves can be changed by a sufficient dose of chloroform from a rise of pressure into a fall. He has in fact shown that chloroform converts pressor into depressor reflexes in the rabbit, and that in this change it alters reflex excitation of vaso-constrictors into reflex inhibition[2]. v. Cyon[3] had previously pointed out that the common crediting of the ordinary afferent nerves of the rabbit with depressor effects on the arterial pressure, although in the dog their effect is pressor, was due to the observations on the former being usually made under chloral as an anæsthetic.

In experiments on the reflex effect of ordinary afferent nerves on skeletal muscle, using the contraction or relaxation of the latter as index of the reflex action, it was found[4] that reflexes of inhibitory effect on the knee-extensor muscle (cat, dog) are changed by a small dose of strychnine so as to become excitatory instead of inhibitory and thus produce contraction in place of relaxation. A similar action of strychnine has been demonstrated by Bayliss[5] in regard to the blood-pressure reflexes in the rabbit. In the observations on the skeletal muscles it was further found that the alterations by strychnine of inhibitory reflexes into excitatory could be undone by chloroform or ether[6]. It was shown that with a sufficient dose of either of these agents after the strychnine change had been effected the reflex response can be changed back again from contraction to inhibitory relaxation once more. On allowing the chloroform narcosis to partially pass off

[1] This *Journal*, XIV. p. 316. 1893.

[2] *Roy. Soc. Proc.* LXXX. B. p. 375. 1908.

[3] *Bull. d. Acad. d. Sci. de St Pétersburg*, Dec. 22, 1870.

[4] Sherrington. This *Journal*, XXXVI. p. 203. 1907; and *Roy. Soc. Proc.* LXXVI. B. p. 288. 1905.

[5] *Roy. Soc. Proc. loc. cit.*

[6] Sherrington. This *Journal, loc. cit.*

the strychnine influence reappears and on then once more sufficiently increasing the chloroform dosage reflex contraction again replaces reflex relaxation. These contrary changes can be repeated a number of times in succession.

The influence of chloroform upon reflexes exciting contraction of the extensor muscle we have now examined further in the following manner. As described in a recent paper[1], we found that in the decerebrate preparation (cat), where the knee-extensor (vasto-crureus muscle) exhibits marked tonus, stimulation of various afferent nerves of the ipsilateral limb produces in many cases, if the stimulation of the afferent nerve be quite weak, a reflex contraction of the muscle, although when stimulation is moderate or strong it produces reflex inhibition. Given a preparation in which the weak stimulation produces reflex contraction we have sought whether, the stimulation of the afferent nerve being repeated without change in its intensity, a simple increase of the dose of chloroform would change its character from excitation and contraction into inhibitory relaxation. A difficulty besetting the observation is that increase of the chloroform is attended by progressive decline of the tonus of the muscle. This decline tends to obscure the observation of an inhibitory effect in two ways. The myograph line instead of running horizontal slopes downward somewhat steeply and there is difficulty in distinguishing a weak inhibitory relaxation from the narcosis relaxation then in progress. Further, if the narcosis has advanced to the degree of altogether abolishing the reflex tonus no background of contraction remains against which inhibitory relaxation can manifest itself. We find however that in fact before the narcosis has advanced to this latter stage, and while therefore some tonus although a declining one remains, a repetition of the stimulus which previously produced reflex contraction does in many instances produce manifest inhibitory relaxation (Fig. 1). We have observed this in the case of the knee-extensor muscle when using the following ipsilateral nerves as afferents for the reflex: popliteal, peroneal, internal saphenous and genitocrural.

The last-named afferent, genitocrural, deserves separate attention because the character of its reflex influence on the knee-extensor presents points of difference[2] from that exerted by the other afferents mentioned. Its peripheral distribution is to the inguinal region, and to the scrotum in the male; hence it is strictly speaking hardly to be reckoned with the other afferents mentioned as belonging to the limb

[1] Sherrington and Sowton. *Roy. Soc. Proc.* LXXXIII. B. p. 435.

[2] Sherrington. This *Journal*, XL. p. 53. 1910.

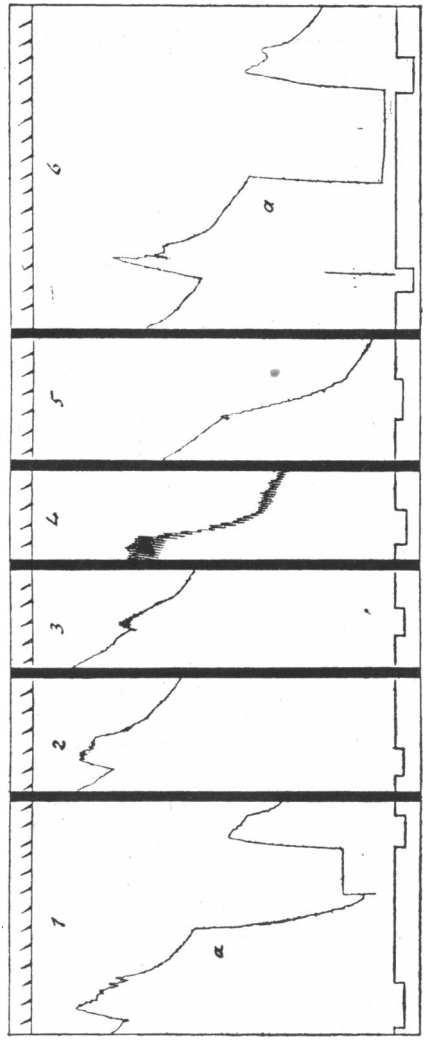

Fig. 1. Time in secs. above. Signal below with downward notch indicating duration of stimulation. The myogram indicates contraction by ascent, relaxation by descent. The base line of the myogram is descending obliquely while the muscle is at rest because the chloroform is decreasing the tonic contraction of the muscle. In piece No. 1 of the tracing the stimulus causes this descent to be broken by distinct contraction and this is so both when the muscle tonus is keeping the muscle partly shortened and when, after being passively extended at *a*, the same stimulus is repeated. The chloroform was taken off between tracings 5 and 6, and the latter shows the return of the reflex to its original character after the chloroform has passed off.

Vasto-crureus preparation. The stimulus was faradism applied to the popliteal nerve and was of the same intensity and frequency throughout.

proper at all. Further, whereas the afferents of the limb proper all readily and constantly under ordinary circumstances produce reflex inhibition of the knee-extensor, the genitocrural under similar circumstances usually produces reflex contraction of that muscle and only occasionally produces reflex inhibition of it. In our present experiments we could in most cases find no strength of stimulation with which it evoked inhibition of the muscle. But it does sometimes do so. In a series of observations on altogether nineteen preparations,

including some previously reported, the stimulation of this afferent evoked reflex contraction of the extensor muscle in all, but complicated in two individuals by occasional replacement of the reflex contraction by distinct inhibitory relaxation. This afferent also differs from the others mentioned in producing contraction as its reflex effect on the knee-extensor even in the decapitate preparation, whereas the others so far as we have seen produce reflex contraction of that muscle only in the decerebrate, *i.e.* fully tonic preparation. It is noteworthy therefore that in the case of the genitocrural with its marked predominance of excitatory over inhibitory reflex effect on the extensor muscle chloroform, or ether, when pushed, produces a change of reflex state in which the stimulus that otherwise produces reflex contraction produces instead of that a reflex relaxation (Fig. 2). We have however not been able to obtain this change in every case in the instance of this nerve; the chloroform sometimes suppresses all reflex reaction without inducing an interim condition characterised by reflex inhibition.

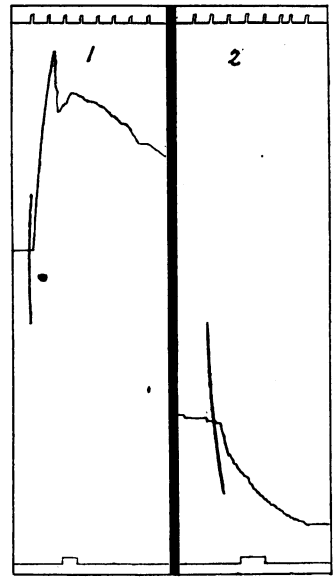

Fig. 2. Time in seconds above. Signal below with upward notch indicating duration of stimulation. The myogram indicates contraction by ascent, relaxation by descent. In piece No. 1 of the tracing, before chloroform, the stimulus causes contraction of the muscle. In piece No. 2, after chloroform, the same stimulus causes relaxation. The difference in level of the starting point of the two responses is a measure of the fall of tonus brought about by the action of the drug.

Vasto-crureus preparation. The stimulus was faradisation applied to the genitocrural nerve and was of the same intensity and frequency in both observations.

Instances begin to be numerous in which the sense of the reflex elicitable from one and the same afferent nerve is seen to be reversed on alteration of some one definite factor in the conditions of the reaction. The change brought about by chloroform is an example of such reversal. But these changes of reaction are separable into two groups according as (1) the determinant alteration lies in conditions attaching purely to the stimulation of the afferent paths or (2) to some other part of the

reflex, for example the central mechanism. Belonging to the former group is the change of movement of the hind limb of the spinal dog from flexion to extension when the stimulus applied to the sole is changed from a nociceptive to a tactual one innocuous in character[1]. To the same group also belong the reversals observed and studied by Fr. Fröhlich[2] and his co-workers[3] in Verworn's laboratory on stimulation of the afferent nerves and afferent spinal roots of the frog. In these Fröhlich distinguishes two categories. In one category the afferent nerve like the nerve of the opening muscle of the arthropod claw[4] evokes a reflex contraction of the muscle when its stimulation is weak or relatively infrequent, but evokes relaxation when the stimulation is strong or of relatively high rhythmic frequence. We have recently shown[5] that in the cat the afferent nerves of the hind limb in respect to their reflex action on the extensor muscle of the knee give results of this type. Under the other category distinguished by Fröhlich come afferent nerves which like the nerve of the closing muscle of the claw evoke, though in the case of the afferent nerves of course reflexly, inhibition when their stimulation is weak but contraction when their stimulation is strong.

Turning to the other class of reversals, namely those which result apart from any change either of intensity or quality in the stimulation of the afferent nerve, a well-known instance is the *umkehr* observed by v. Uexküll[6] in invertebrates and by Magnus[7] in the mammal. In these under identical stimuli a passively imposed change in the posture of the appendage (ray, tail, limb) diametrically alters the sense of the resulting reflex movement. And Magnus[8] has traced this result to an influence exerted by the change of posture upon the central mechanism of the reflex. Other instances also belonging to this second large group, the sense of the reflex effect being changed diametrically though the stimulus to the afferent nerve remains wholly unaltered, are the reversals given by strychnine and chloroform. The strychnine reversal has been observed with the reflex inhibitions of extensor muscles[9], with

[1] Sherrington. This *Journal*, xxx. p. 39. 1903.

[2] *Zeits. f. allg. Physiol.* 1909, ix. p. 85.

[3] Tiedemann. *Zeits. f. allg. Physiol.* 1910, x. 183. Veszi. *Zeits. f. allg. Physiol.* 1910, ix.

[4] C. Richet. *Arch. de Physiol.* 1879. Biedermann. *Sitzungsb. d. k. Akad. d. Wiss. Wien.* 1887. Fr. Fröhlich. *Zeitsch. f. allg. Physiol.* vii. 1908.

[5] *Roy. Soc. Proc.* lxxxiii. B. p. 435.

[6] *Zeitsch. f. Biol.* 1897, xxxviii.

[7] *Pflüger's Arch.* 1910, cxxv.

[8] *Pflüger's Arch. ibid.*

[9] Sherrington. *Op. cit.*

depressor reflexes on blood-pressure[1] and with the expiratory reflex from ammonia which becomes inspiratory[2]. The chloroform reversal, which is of opposite sense, has been observed with pressor reflexes on blood-pressure[3]; the observations in this paper show that it can be traced also in reflexes expressed by the skeletal muscles.

[1] Bayliss. *Op. cit.*
[2] J. Seemann. *Ztsch. f. Biologie*, LIV. 153. 1910.
[3] Bayliss. *Op. cit.*