gradually declined. A curve of the average daily temperatures of these dogs does not differ significantly from the curve of all 30 dogs in the group as shown in Fig. 1. The other 7 dogs of this group had no significant initial rise in temperature but developed a late elevation about the 18th to 22nd day. In these 7 dogs the larger dose of 15 mg produced temperature reactions somewhat similar to those produced by the smaller dose.

Previous reports[5] have recorded the low pathogenicity of ferret-passage virus. In the present experiments, 1 dog of the 50 injected with 54th-generation virus was destroyed on the 14th day, and 1 of the 60 injected with 63rd-generation virus was destroyed on the 15th day when they developed prolapse of the rectum. One dog injected with 63rd-generation virus died in convulsions on the 5th day, but the fatality did not seem to be related to the inoculation.

Conclusions. Ferret-passage distemper virus of 54 serial transfers, upon injection into young dogs, induced a mild infection with a biphasic temperature reaction similar to that observed in natural distemper infections. No difference in temperature reactions was observed in groups of dogs injected with 2.5 mg and with 15 mg of the ferret-passage virus. Similar mild reactions were observed following the injection of virus of 63 ferret passages. The dose of 2.5 mg produced temperature reactions which were biphasic in character. The 15-mg dose of this virus tended to produce an exaggerated initial fever which gradually declined without the production of a second rise in temperature.

[5] Green, Robert G., *Am. J. Hyg.*, 1945, **41**, 7.

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The Influence of Muscle Pain on Spinal Reflexes.*

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Introduction. In a previous investigation[1] the effect of intramuscular injection of NaCl solution on the response of the motor cortex to electrical stimulation has been studied. It was shown that the effect of cortical stimulation was altered quantitatively and qualitatively under these conditions. Since evidence from our own experiments based on reflex effects, particularly on the pupil, as well as from studies of Lewis,[2] on man, suggested that injection of hypertonic NaCl solution caused "muscle pain," the experiments were interpreted to mean that "muscle pain" altered the effect of cortical stimulation of the motor area on the organism. The physiological mechanism involved in these reactions has not yet been determined. As a first step in this direction experiments are reported in this paper in which the influence of "muscle pain" (*i.e.*, of stimuli known to cause muscle pain in man and to induce pupillary dilatation and vocalization in anesthetized animals) on spinal reflexes was investigated.

Method. The experiments were performed on eleven cats and one macaque. .45 cc dial-urethane (Ciba)† /kilo was injected intraperitoneally. The knee jerk was elicited every two seconds by means of a device similar to that described by Johnson.[3] The flexor reflex (tibialis ant.) was studied by means of condenser discharges applied at intervals of 2.5 seconds. In some of the animals studied the spinal cord was transected at the first lumbar level. As stimuli which result in muscle pain

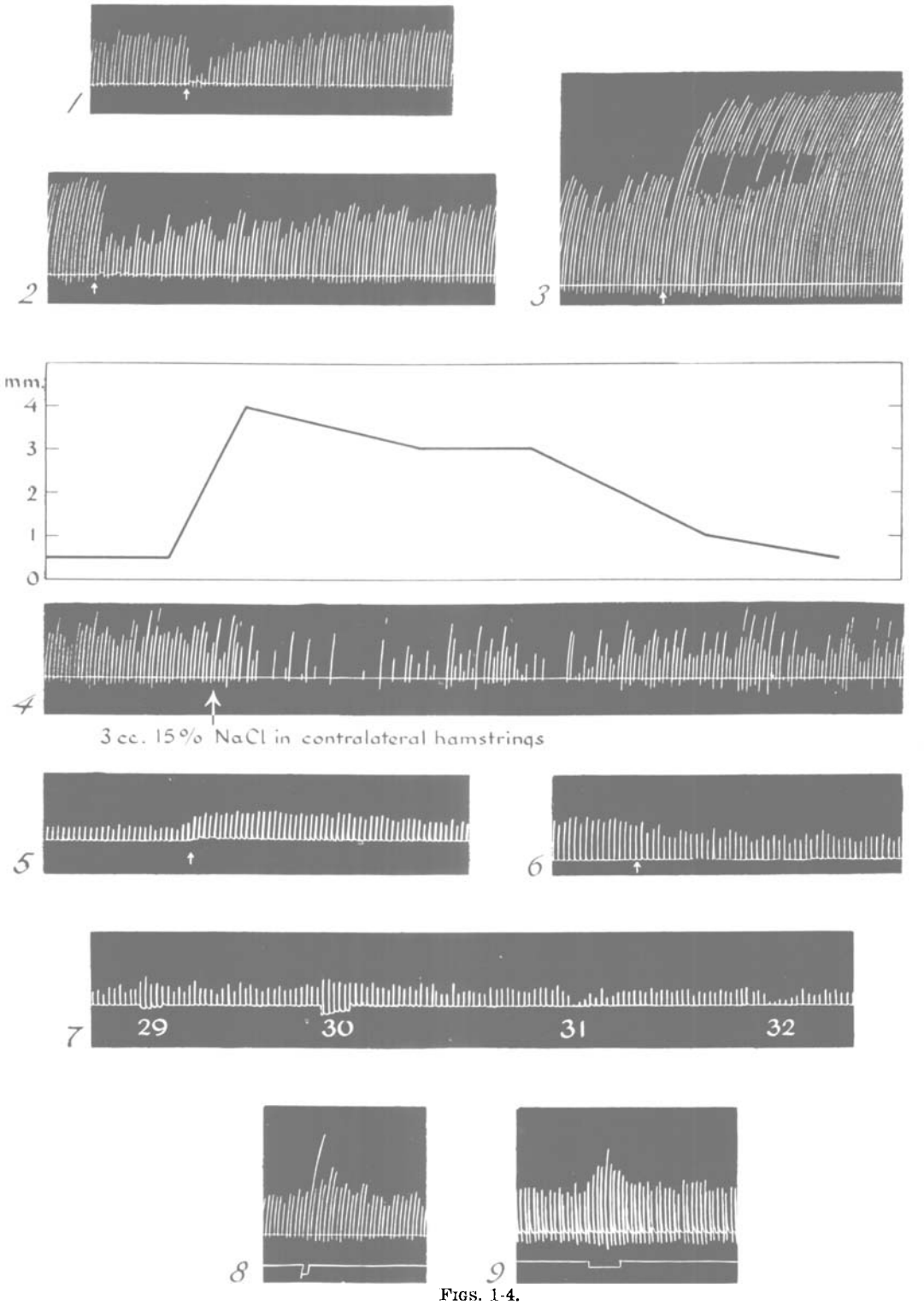
* Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

[1] Gellhorn, E., and Thompson, L., *Am. J. Physiol.*, 1944, **142**, 231.

[2] Lewis, T., *Pain*, New York, 1942.

† Ciba Pharmaceutical Products, Inc., was kind enough to donate this drug.

[3] Johnson, C. A., *Am. J. Physiol.*, 1927, **82**, 75.



FIGS. 1-4.

Knee jerk elicited every two seconds in cats anesthetized with .45 cc dial-urethane. At the arrow 15% NaCl was injected intramuscularly as follows:

Fig. 1, 2 cc into ipsilateral hamstrings; Fig. 2, 1 cc ipsilateral hamstrings; Fig. 3, 2 cc contralateral gastrocnemius; Fig. 4, 3 cc contralateral hamstrings. The graph above the knee jerk record of Fig. 4 shows the change in pupillary diameter resulting from the injection of hypertonic NaCl solution.

FIGS. 5, 6, 7, AND 9.

Flexor reflex (tibialis ant.) of the cat anesthetized with dial-urethane was elicited by condenser discharges applied at intervals of 2.5 sec. to the central end of the sciatic ipsilateral (intensity 5-6 volts). At the arrow 2 cc 15% NaCl were injected intramuscularly into the ipsilateral hamstring (Fig. 5) and 3 cc of this solution into the contralateral hamstrings (Fig. 6). Fig. 7 shows the effect of faradization of muscles on the flexor reflex. Nos. 29 and 30 ipsilateral faradization of the quadriceps at 11 and 9 cm c.d. respectively. Nos. 31 and 32 contralateral faradization of the gastrocnemius at 9 cm c.d. Fig. 9: Effect of faradization (6.5 cm c.d.) of the ipsilateral quadriceps on the flexor reflex.

FIG. 8.

Macaque .55 cc dial-urethane/kilo i.p. Effect of faradization (6 cm c.d) of the contralateral quadriceps on the knee jerk.

in man we used injection of 15% NaCl solution or faradization of ipsi- and contralateral muscles.

Results. The experiments showed that the injection of 15% NaCl as well as the faradization of muscles influence the knee jerk and the flexor reflex of cat and monkey. Fig. 1 and 2 demonstrate the effect of injection of a hypertonic NaCl solution into the ipsilateral muscles on the knee jerk. This reflex is regularly depressed under these conditions, but the effect may vary greatly in intensity and duration as shown in these figures. It may, however, be emphasized that apparently due to the slowness of diffusion processes the effect resulting from the injection of hypertonic solutions may persist for several minutes. It is reversible and accompanied by dilatation of the pupil and, in some instances, by vocalization. When NaCl was injected into muscles of the contralateral side the results were not uniform. In seven experiments an increase in the knee jerk was observed whereas in three experiments the knee jerk was actually diminished. Examples for the two types of results are shown in Fig. 3 and 4. Contralateral injection of NaCl caused a distinct increase in the knee jerk in Fig. 3, whereas in Fig. 4 it was accompanied by a prolonged inhibition of this reflex.

As was mentioned in the introduction, faradization of muscles likewise causes muscle pain in the human. Therefore this stimulus was used in order to study its effects on the knee jerk. It was found that ipsilateral faradization inhibited the knee jerk whereas contralateral muscle faradization increased the effect. These effects were temporary and lasted only as long as the stimulus was applied. Neither the injection of NaCl nor the faradization of the muscle caused in themselves, a reflex on the recorded muscle.

In a second group of experiments the effect of these stimuli on the flexor reflex was studied. Fig. 5 and 6 illustrate the action of ipsi- and contralateral injection of hypertonic NaCl solution on the flexor reflex. Whereas ipsilateral "muscle pain" increases the flexor reflex, contralateral "muscle pain" decreases it. This statement applies for the "muscle pain" resulting from the injection of hypertonic NaCl solution (Fig. 5 and 6) as well as for the faradization of muscles (Fig. 7). It is apparent from the description of these experiments that in general the extensor reflex (knee jerk) and the flexor reflex react in opposite manners to the same type of stimulus. This is further illustrated by Fig. 8 and 9 in which it is shown that contralateral faradization increases the knee jerk in a similar manner as ipsilateral faradization effects the flexor reflex. The converse statement is likewise true but an illustration has been omitted.

Discussion. Since the effects described in the preceding paragraphs were obtained in animals with the spinal cord transected at the lumbar level as well as in animals with the spinal cord intact, it may be inferred that they represent effects on the spinal centers. It seems therefore justified to conclude that osmotic or faradic stimulation of pain fibers in the muscle leads to an alteration of the excitation of spinal centers which is demonstrated by marked changes in spinal reflexes in response to a standard stimulus. Although the stimuli used in these experiments led, in

many instances, to profound alterations of the reflexes for several minutes, they did not cause any reflexes by themselves. However, they acted, in general, as was to be expected if Sherrington's rules could be applied to nociceptive stimuli although the latter did not evoke any reflexes. Since ipsilateral nociceptive stimuli elicit flexor- and inhibit extensor-reflexes whereas contralateral stimuli act in opposite manners ipsilateral nociceptive stimuli may be expected to increase flexor- and decrease extensor- (knee jerk) reflexes, and opposite effects should be produced by contralateral nociceptive stimuli. Our results show that this is, in general, the case. However, it is worthy of mention that, in several instances, contralateral stimulation of pain fibers by means of hypertonic NaCl solution markedly diminished the flexor reflex. The prolonged and sometimes considerable increase in pupillary diameter which accompanied this inhibitory effect (*cf.* Fig. 4) makes one suspect that this deviation from the rule occurred particularly when excessive pain was induced.

It was shown earlier (Gellhorn and Thompson, 1944) that the effects of electrical stimulation of the motor cortex were greatly increased by means of painful stimuli applied to the muscles of the limbs. In contradistinction to the influence of "muscle pain" on spinal centers described in this paper it was found that its action on the effect of cortical stimulation was independent of the "laterality" of the pain stimulus. Thus cortical stimulation of the left motor area lead to an intensification of the movement of the right foreleg after injection of hypertonic NaCl solution in either the right or the left hindleg. Apparently the alteration of the effects of cortical stimulation as a result of "muscle pain" is not simply the result of the action of these painful stimuli on spinal centers, although these centers are likewise profoundly influenced.

Summary. Stimuli such as injection of hypertonic NaCl solution into striated muscle or faradization of muscles which cause "muscle pain" in man, and pupillary dilatation and vocalization in the anesthetized animal modify spinal reflexes in the latter. It is shown that in general ipsilateral "painful" stimuli increase the response of a flexor reflex and diminish the response of the knee jerk to a standard stimulus. On the other hand, contralateral "pain" stimulation causes an increase in the knee jerk and a decrease in the flexor reflex. If excessive stimuli are used the knee jerk may be inhibited not only from the ipsi- but also from the contralateral side. The fact that "muscle pain" greatly enhances the effect of electrical stimulation of the motor cortex is not due to the alteration of spinal centers but suggests the involvement of supraspinal mechanisms.

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Effect of Tobacco Virus, Some Decomposition Products of Nucleoproteins, and Related Compounds on Acetylcholine Synthesis.*

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In the presence of serum,[1,2] spinal fluid,[3] and thymus[4] from patients with myasthenia gravis less acetylcholine was synthesized *in vitro* than in the presence of similar tissues

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[1] Torda, C., and Wolff, H. G., *Science*, 1943, **98**, 224.

[2] Torda, C., and Wolff, H. G., *J. Clin. Invest.*, 1944, **23**, 649.

[3] Torda, C., and Wolff, H. G., *Science*, 1944, **100**, 200.

[4] Trethewie, E. R., and Wright, R. D., *Australian and New Zealand J. Surg.*, 1944, **13**, 244.