612.833.7

STATE OF THE FLEXOR REFLEX IN PARAPLEGIC DOG AND MONKEY RESPECTIVELY.

By J. F. FULTON and C. S. SHERRINGTON.

(*From the Physiological Laboratory, Oxford.*)

Marked difference of reflex activity obtains between the paraplegic dog or cat on the one hand and the paraplegic monkey on the other. For instance, the flexor reflex of the hindlimb in the spinal dog and cat is facile and vigorous, in the monkey difficult or impossible to evoke. This diversity is important because evidently correlated with the relative distances respectively separating these two mammalian types from that of man. We have sought to find numerical expression for this, and thus to get a numerical grading for the difference of spinal condition which it represents.

Method.

The upper limit of the share of a particular muscle which a given excitatory reflex has at command can for some muscles and some reflexes be ascertained fairly closely by the isometric myograph. That upper limit, peripheral conditions afferent and efferent remaining equal, can serve as test for the central effectiveness of the reflex. To such a test the flexor reflex, sampled by the main ankle flexor, tibialis anticus, lends itself well. It is a reflex in which frequency of reflex discharge tends to correspond with frequency of the sensory stimulation of the afferent nerve; hence the muscle can be reflexly driven at the same rate as the motor tetanus against which it is to be calibrated.

The tibialis anticus is "isolated" for the myograph by putting out of action by nerve section or tendon resection all other muscles of the limb. The limb is fixed by steel drills through upper and lower ends of the tibia and clamped to the table below the myograph. The myograph used was of the torsion bar type fitted with a mirror for registering optically. In one experiment the torsion element was a steel strip [Hartree and Hill, 1921], in the others it was a torsion wire with a rocking knife-edge bearing [Eccles and Sherrington, 1930], with the mirror axially set on the free end of the torsion element. The afferent nerve was the ipsilateral popliteal in the thigh; the motor nerve was the peroneal, all branches except that to tibialis being cut distally. Observations were made on the dog, cat and common macaque monkey. In the former the cord was in every case cut between 9th and 10th thoracic segments: in one monkey the cord was at 11th thoracic, in the other three at 8th thoracic

segment. Where the myographic examination was made within a few hours of the severance of the spinal cord, the procedure was, before relaxing the anæsthesia employed during the operation on the cord, to decerebrate, and then forthwith to discontinue the anæsthetic. Then 3–4 hours later the myographic examination was undertaken. Records were made of (1) the reflex at its strongest, (2) of the maximal motor tetanus. The samples of these were usually taken alternately, the motor nerve being stimulated in its continuity.

Results.

The experiments fall into two groups: (1) where the myographic examination was made 3–4 hours after spinal transection; (2) where it was made not earlier than the 21st day after the transection. These latter are marked *c* (*i.e.* "chronic") in the accompanying table.

Table. Contraction tension in g.

	Wt. in kg.	Reflex	Motor	Reflex as p.c. of motor
Dog	7·5	3490	4330	82
„ *c*	6·3	3250	3660	88
Cat	—	2510	3150	80
„	—	1750	2220	79
„ *c*	2·1	1800	2140	84
Monkey	3·6	0	3920	0
„	3·2	? 10	3450	0
„	1·8	0	3950	0
„ *c*	2·5	95	210	46

Where the observations were taken within a few hours after cutting the cord the value obtained for the reflex both in dog and cat agreed fairly with results observed in the cat and recorded in a former paper [Cooper, Denny-Brown and Sherrington, 1926]. There the value was 77 averaged from 4 cats; here 79·5 for the cats and 82 for the dog. Against those figures two of the three monkeys gave 0, and the third less than 0·5, an extreme contrast.

(1) Evidently in the early "acute spinal" state the spinal activity of the mammalian type less remote from man is, as judged by this reflex, vastly inferior to that of the type more remote from man. The extensor reflexes it is true are in the "acute spinal" dog and cat much more depressed [Sherrington, 1910] than is the flexor reflex which is freed from prespinal inhibition [Sherrington and Sowton, 1915]. With the extensor reflexes therefore the inequality between dog and monkey is hardly so marked, although with them also the reflex inactivity of the early "acute spinal" state is greater in the monkey than in the dog and cat, witness the frequent total abeyance of the knee jerk even for days in the "acute spinal" monkey.

(2) The reflex activity of the isolated cord tends to show some pro-

gressive increase for periods covering days and weeks and even months. Our observations were therefore extended to see how far the great difference obtaining between dog (and cat) and monkey in the "acute" experiments would hold also over longer periods. The myographic examination was conducted subsequent to complete healing of the operation wound, the spinal severance having been performed with full precautions for asepsis. In each case the general health of the animal was, apart from the condition of paraplegia, good.

Dog, small; 7. xii. 29; 10th thoracic spinal segment excised. Wound healed rapidly. Animal remained in good health. Usual reflex activity; stepping of hindlimbs on being raised; bilateral active extension of hindlimbs on first allowing the limbs to hang pendent. 2. vi. 30. Weight 6·3 kg.; anæsthetized and decerebrated at 10 a.m.; limb prepared, and myographed at 2.30 p.m. Results see Table.

Cat, young; 24. iv. 30, cord cut at 10th thoracic. 1. viii. 30. The wound had healed quickly and the general health has remained good, and animal has grown; weighs 2·1 kg. Reflexes; spring clip to hindfoot excites quick and prolonged flexion reflex, with some stepping of opposite hindlimb. The flexion reflex under persistence of the stimulus tends to break into irregular alternating movements including adduction-abduction of limb, as if to liberate the limb from the stimulus. Light touching of the toepads or plantar cushions evokes lifting and spreading of the toes. When spinal stepping is in progress light passive support of one thigh in its descent toward extension stops the stepping in both limbs. At 10 a.m. decerebrated under anæsthetic. Limb prepared: myographic examination at 3 p.m. Results see Table.

Monkey, *Macacus rhesus*; 2. vii. 30, forenoon, cord transected at 8th thoracic segment, under dial. 9. vii. 30. Wound has healed well: feeds well and has done so since late afternoon of 3rd. Complete flaccid paraplegia of hindlimbs; no reflexes; slight decubitus ulcer on right hip. 14. vii. 30. Feeding well, and is lively. No knee jerk; adductor response to tapping tendon; slight flexion of hallux on pinching toes. Some ulceration on right hip; extensive wasting of muscles; no trouble with bladder; rectal temp. 37°C. 19. vii. 30. Wasting of hindlimbs more marked; knees and ankles stand out like knobs in the flaccid limbs. Belly wall relaxed; no knee jerks, but adductor jerks present. Flexion of hallux on pinching foot, accompanied by slight flexion of ankle. Feeds well; is very active with forelimbs; ulcer still present over right hip; temp. normal. Photographed.

22. vii. 30. Good general condition apart from the paraplegia; no knee jerks; adductor responses on tapping tendon; flexion of hallux on pinching foot. The small sore over trochanter is covered with clean granulation tissue and has not led to general infection; no induration of surrounding muscle. Wasting of hindlimb muscles is extreme. Afternoon: myographed. As the animal showed no sensation whatever at any point below 8th thoracic level no general anæsthetic was used: an assistant merely nursed and amused the animal while the hindlimb (left) was prepared. Tetanization of central ipsilateral popliteal nerve gave sluggish retraction of the cut tib. ant. tendon which lay free; also evident contraction of the adductor of opposite thigh. In the myograph the threshold for tib. ant. reflex from popliteal was 11·5 cm. (coreless coil) and at 10 cm. had reached its maximal effect, *i.e.* 95 gm. contraction tension. Tetanic stimulation of uncut peroneal nerve (its branches except that to tibialis anticus having been cut peripherally) gave threshold for motor response at 15·5 cm. and was maximal at 12·5 cm. giving 210*g.* contraction tension. The motor and reflex responses were taken approximately alternately. The tetanic contractions

relaxed very sluggishly, the "motor" tetani quite as slowly as the "reflex." The "latent period" of the reflexes was always very long, *i.e.* between 80σ and 90σ. To test possible escape of current for reflex stimulus at 10 cm. the electrodes remaining as placed on popliteal the peroneal was then cut proximal to the anatomical meeting point of the two nerves; the response from popliteal then entirely disappeared; it was therefore wholly reflex. Single break shock stimuli then applied to distal peroneal found motor threshold at 15·9 cm. and maximal at 12·5; the maximal twitch reached 100 g. tension. The twitches like the tetani showed quite abnormally slow time relations (*v. infra*).

Necropsy showed complete and clean spinal severance at 8th thoracic; the opposite face of the cut cord were 3 mm. apart, with some young scar tissue between them. The cord appeared healthy to naked eye except for obvious "tract" degeneration detectible to close inspection above and below the lesion.

Discussion.

The myograph showed the flexor reflex both in dog and cat to have a distinctly higher value in the "chronic" spinal condition than in the "acute," 88 and 82 as against 80 or a little less. It was not clear from the few experiments that the power of the "motor" tetanus itself falls in those animals in the "chronic" spinal condition necessarily far below normal; but in the "chronic" monkey a peripheral change was met with, impairing the nerve-muscle complex itself. This peripheral impairment was a complication for the evaluation of the reflex. The occurrence of muscular wasting even of dystrophic character in the paraplegic limbs had not been unexpected [Sherrington, 1898; McCouch, 1924]. McCouch in his observations in the monkey found microscopic changes (advanced chromatolysis) in the ventral-horn cells of the spinal grey matter of the limb region accompanying a severe paraplegic state of 35 days' duration. As to the human cord, Dr Gordon Holmes writes us from first-hand experience that he has repeatedly observed chromatolysis in the motor-horn cells below severe transverse lesions. We found in our 3 weeks' monkey the contraction responses of the flexor muscle under direct stimulation of its motor nerve to be in fact severely defective and abnormal [cf. also Matthes and Ruch, 1931]. The maximal twitch of tibialis anticus for a monkey of the kind, age and weight we were using should, to judge from the other three monkeys of the series, be about 900 g., whereas the value found (Fig. 1) was 105 g., nearly a 90 p.c. deficit. The ratio twitch tension/tetanic tension proved abnormally high 45/100, instead of about 28/100 as would be expected. For the motor tetanus the subnormality of tension was therefore even greater than for the twitch. The enfeeblement of the response and the wasting of the muscle were more than mere disuse could account for. Moreover the time relations of the contractions were grossly abnormal. The twitch had, following the nomenclature of

Cooper and Eccles [1930], a "contraction time" of 140σ, *i.e.* took that time to reach its maximal tension; and the whole twitch lasted some 900σ. The maximal tetanus took nearly a second to relax. In *Macacus rhesus* normally this muscle has a contraction time of barely 30σ, and reaches complete relaxation in about 210σ (Fig. 1). The weight of the tibialis anticus muscle in the paraplegic monkey of 3 weeks' standing was 2·8 g., whereas in a normal *Macacus rhesus* of rather lighter body weight the tibialis anticus weighed 5·5 g. Miss Cooper kindly compared the maximal twitch tension of tibialis anticus of a normal *Macacus rhesus* (1·8 kg. body weight), the muscle with its tendon weighing 5·6 g., with that of a

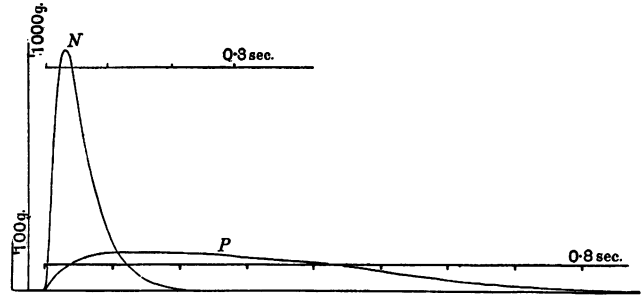

Fig. 1. Isometric records of maximal motor twitch of tibialis anticus of monkey *P*, *M. rhesus*; 2·4 kg. body weight; 3 weeks' paraplegic; *N*, *M. rhesus*; 1·8 kg. body weight; normal. Separate tension scales for *P* and *N* to left; times as abscissæ.

tibialis anticus weighing 4·8 g. from a 2·4 kg. cat. The monkey's tibialis gave for maximal twitch 1040 g. tension, the cat's 720.

Our monkey's reflex had therefore a defective nerve muscle to take expression through. If that be considered not to invalidate the application to this case of the test used in the others for evaluation of the amount of reflex, then the reflex in this case can be graded at 45. In support of accepting the figure, as an approximation, is the circumstance that both elements of the ratio, the "reflex" and the "motor" are measured through the same deteriorated nerve-muscle preparation. The importance of the value thus obtained is that although much smaller than in dog (and cat) it is nevertheless much larger than that obtained in the monkey in the "acute" spinal state. This argues that there does exist in the hindlimb of the monkey a spinal flexor reflex, although immediately subsequent to hind thoracic severance of the cord it is so enfeebled as to be not then obtainable. That there is some degree of variability from experiment to experiment in regard to this enfeeblement is likely; our two observations indicate that. The spinal knee jerk is similarly variable. In

the second and third monkeys of our series the spinal transection, at 8th thoracic level, was not followed by disappearance of the knee jerk. The knee jerk was feeble but remained present even from immediately after the performance of the transection. This is unusual [Fulton, 1932; Sherrington, 1898]; and in the first and fourth monkeys of our series, although of the same species and age, the knee jerk was absent after the transection, and in the fourth animal did not return during the subsequent 3 weeks.

Summary.

1. In the monkey (*Macacus rhesus*) after spinal transection in the thoracic region the flexor reflex of the hindlimb instead of being facile and vigorous as in the dog (and cat) is for a time unobtainable or if obtainable is so merely as a trace.

2. In the course of some weeks in monkey, as in dog (and cat), there ensues some increase of the reflex, the reflex in the monkey can become distinctly elicitable, but in the monkey there supervenes a peripheral condition of wasting and deterioration of the nerve-muscle response ("isolation dystrophy"), which tends to obscure observation of such central reflex action as exists by impairing its means of expression.

REFERENCES

Cooper, S., Denny-Brown, D. and Sherrington, C. S. (1926). *Proc. Roy. Soc.* B, **100**, 448.
Cooper, S. and Eccles, J. C. (1930). *J. Physiol.* **69**, 377.
Eccles, J. C. and Sherrington, C. S. (1930). *Ibid.* **69**, 1 *P.*
Fulton, J. F. and Keller, A. D. (1932). *The Sign of Babinski*, in press (Springfield, Ill.).
Hartree, W. and Hill, A. V. (1921). *J. Physiol.* **55**, 389.
Holmes, Gordon M. Personal communication.
McCouch, G. P. (1924). *Amer. J. Physiol.* **71**, 137.
Matthes, K. and Ruch, T. C. (1931). *J. Physiol.* **72**, 29 *P.*
Sherrington, C. (1898). *Phil. Trans. Roy. Soc.* B, **90**, 136.
Sherrington, C. (1910). *J. Physiol.* **40**, 28.
Sherrington, C. and Sowton, S. C. M. (1915). *Ibid.* **49**, 331.