herein described, and the curtailment of exploration and increase of time scores as reported by others[4] are identical in kind. The literature is replete with examples showing that one and the same end-result in terms of reduction of level of activity may be the consequence of many diverse factors. Through factor analysis, van Steenberg[8] found that only a small fraction of the reliability of drum scores can be accounted for by a factor which is common to these and to other performances in mazes, problem boxes, and other tests. Thus, further analyses are needed before one may safely assume that the partial inactivation of rats in the activity drum is effected by the same factors as those which interfere with the exploratory tendency and the increase in time scores on learning tasks.

Summary. A series of daily electro-convulsive shocks in 13 male rats, for 5-day periods, significantly reduced concurrent activity as compared with (1) preshock activity, (2) 5-day periods of no-shock, interposed between periods of shock, and (3) the post-shock recovery period. There is a cumulative effect of successive periods of shock. The mean level of activity reached during the post-shock period of 30 days was significantly lower than that of the preshock period. Whether this difference was due to natural decline of activity with age or to lingering effects of electro-convulsive shock was not determined.

[8] van Steenberg, N. J. F., *Psychometrika*, 1939, **4**, 179.

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A Second Motor Nerve System to Frog Skeletal Muscle.

S. W. KUFFLER.* (Introduced by R. W. Gerard.)

From the Department of Physiology, University of Chicago.

The existence in skeletal muscle of special tonus mechanisms—particular nerve or muscle fibres or contractile elements—has often been proposed and as often been discarded. Tasaki and Mizutani[1] recently reported that stimulation of small diameter nerve fibres could initiate slow contractions in frog muscles. It appears that no electrical investigation of this problem has yet been made, nor have the structures giving slow contractions been identified. The present investigation following Tasaki and Mizutani's study clearly demonstrates a separate neuromuscular system which may well be involved in tonus and contracture and which has been missed because of the much greater action of the well-known twitch system. This latter has been eliminated (a) by progressive pressure block or galvanic block applied to the frog's sciatic below the point of stimulation following Leksell[2] (the large fibres failing sooner) and then observing various leg muscles, or (b) by cutting all but the desired fibre[1] in a small nerve (about 10 fibres) to an isolated toe muscle (extensor longus digiti IV., 15 mm long, 40 to 60 fibres) observed under the microscope.

As compared with the usual motor nerve fibres, those here active are of smaller diameter, higher threshold, greater resistance to pressure or polarization block and slower conduction. They are probably not autonomic, since they may be larger than 5 micra. A single impulse in one evokes a barely visible movement of an attached small muscle, repeated impulses at 3 to 4 a second give a small local shortening and at 20 to 50 a strong slow local contraction appears and in some preparations an occasional fully-propagated

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[1] Tasaki, I., and Mizutani, K., *Jap. J. Med. Sciences*, 1944, **10**, 237.

[2] Leksell, L., *Acta Physiol. Scand.*, 1945, **10**, suppl. 31, 84.

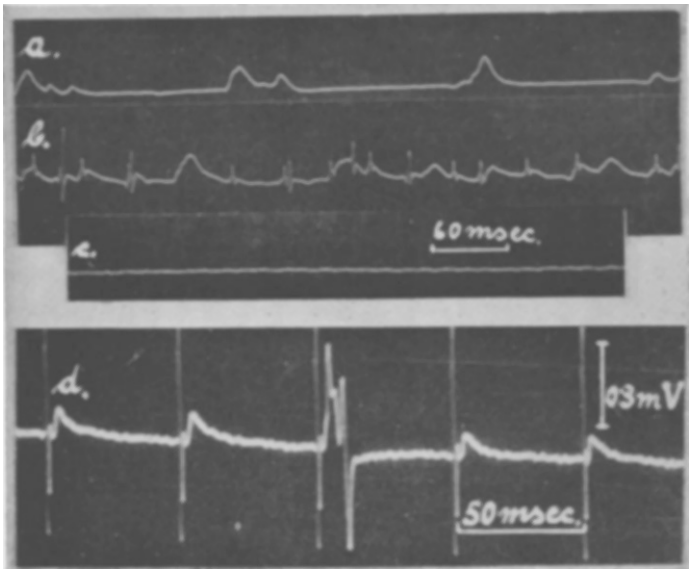

FIG. 1.

a. M. semitendinosus. Spontaneous activity recorded during "rest" in circulated spinal preparation. *b.* Same preparation; activity following on weak reflex excitation (touching of toes). Note increased frequency of local potentials and appearance of some propagated impulses. The latter are accompanied by small twitches. *c.* Activity abolished after cutting nerve supply. *d.* M. extens. long. dig. IV. Potentials set up by stimulation of a single small nerve fiber at 20 per sec. Occasional propagated impulses appeared during this series. Amplification the same in all records.

twitch may also be set up (Fig. 1d). Along with the accompanying potentials the local shortening is limited to the region of the neuromuscular junction.

The local muscle potential resembles the usual endplate potential as obtained after curarization.[3] It appears after a longer interval following stimulation of the nerve, is often slower on rise and fall, and is smaller than the curarized endplate potential. The local potential rises, to a peak of approximately 0.2 mV when excessive short-circuiting is avoided, in 3 to 4 msec. and falls to half in about 13 msec. When recording the activity from the surface of exposed "resting" muscle, local potentials of widely varying time course appear (Fig. 1a). These do not represent the true time course of individual potentials but are a composite effect of multiple scattered units. Repetitive stimulation at 20 to 50 per sec. does not lead to significant local potential facilitation. A similar system of local contractions and potentials has recently been studied in crustacea.[4]

Although the local and propagated muscle responses are so different, the same muscle fibres may be involved in both. The occasional appearance of fully conducted twitch responses with the local potentials on tetanizing of a small nerve fibre has been mentioned (Fig. 1d). Further, dissection of small muscle bundles shows that the muscle fibres are all similar and that the same ones can be excited by "small" and "large" nerve fibres. Both types of nerve endings, therefore, can occur on one muscle fibre. One small nerve fibre can supply multiple groups of endings, each group reaching several muscle fibres in a single area, as revealed by as many as three regions of local potential and shortening.

The local potentials, with or without propagated ones, can easily be obtained from the surface of many leg muscles in the circulated spinal frog. They appear at varying fre-

[3] Eccles, J. C., Katz, B., and Kuffler, S. W., *J. Neurophysiol.*, 1941, **5**, 362.

[4] Katz, B., and Kuffler, S. W., *Proc. Roy. Soc.*, 1946, B 133, 374.

quencies (Fig. 1a,b) depending on the number of sensory impulses reaching the cord from the periphery. They can develop tensions of 10 to 15% of a maximal twitch response. Nerve section abolishes them (Fig. 1c). Mammals have not yet been studied.

Summary. A separate small-nerve motor system to frog skeletal muscles is described. It is active reflexly and may be related to muscle tone. It evokes local potentials and local shortening at the region around the nerve-muscle junctions, in sharp contrast to the propagated twitches and muscle impulses which can be elicited, by the usual motor nerves in the same muscle fibres. Small fibre activity alone may set up appreciable muscle tension.

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Benadryl* Fails to Protect Against the Histamine-Provoked Ulcer.†

STANLEY R. FRIESEN, IVAN D. BARONOFSKY, AND OWEN H. WANGENSTEEN.
From the Department of Surgery, University of Minnesota, Minneapolis, Minn.

It has been shown that synthetic benzhydryl alkamine ethers are capable of preventing fatal asthma induced in guinea pigs by administration of histamine either intravenously or by inhalation of atomized aqueous solution.[1] These drugs also have been demonstrated to be effective in alleviating anaphylactic shock in guinea pigs[2] and dogs.[3] Lowe and his associates also found that the activity of the synthetic benzhydryl alkamine ethers equaled or exceeded that of the 2 Fourneau histamine antagonists, thymoxyethyldiethyl amine (929F) and N-phenyl-N-ethyl-N'-diethylenediamine (1571F).[2] The latter drugs (929F) and (1571F) have been shown to produce no alteration of gastric response to histamine in Heidenhain pouches in dogs.[4,5]

Of the various synthetic benzhydryl alkamine ethers, β-dimethylaminoethyl benzhydryl ether hydrochloride (benadryl) was found to be the most potent histamine antagonist in alleviating anaphylactic shock and histamine-induced asthma in guinea pigs.

The effect of benadryl on the action of histamine as judged by blood pressure changes has been studied.[6] It was found that benadryl given intravenously in the amounts of 3 mg per kg body weight abolishes the fall in blood pressure in dogs produced by 0.001 to 0.002 mg per kg body weight of histamine. In that study, the amount of histamine "antagonized" by given doses of benadryl was quantitated and the mechanism of this "antagonism" was stated to be owing to the adsorption of benadryl onto the site of action of histamine, a circumstance which Wells and his associates believes disturbs the histamine equilibrium such that a given amount of his-

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2 Loew, E. R., and Kaiser, M. E., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 235.

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4 Burchell, H. D., and Varco, R. L., *J. Pharm. and Exp. Therap.*, 1942, **75**, 1.

5 Hallenbeck, C. A., *Am. J. Physiol.*, 1943, **139**, 329.

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