that stretching causes an increased rate of conduction of a circus wave. As soon as the rate of stimulus formation reaches values of approximately 600 per minute the appearance of refractory islands of muscle makes a regular response impossible and flutter changes into fibrillation.

The appearance of fibrillation following stretching, particularly on stretching by intravenous infusion (Fig. 4b) is of interest because it may explain the attacks of paroxysmal fibrillation on sudden physical exertion. The increased filling of the right auricle particularly at the beginning of sudden severe physical exercise[10] may in a predisposed heart elicit paroxysmal fibrillation.[11-13]

We fully appreciate the fact that the assumption of a rapid stimulus formation as the cause of auricular flutter or fibrillation[2] will necessitate an answer to one pertinent objection: Why does stimulation of the vagus nerves increase the auricular rate of one type of auricular tachycardia (auricular flutter) and stop the stimulus formation during sinus rhythm or other auricular tachycardias? Auricular extrasystoles caused by the intravenous injection of minute doses of aconitine disappear during the faradic stimulation of the vagus nerves. They increase in number after the stimulation of the vagus is discontinued.[14] At the present time we are not prepared to offer an explanation for this fundamental difference. It is possible that local application of aconitine causes the establishment of a continuous stimulus; this would elicit more frequent responses with a shortening of the refractory phase during stimulation of the vagus nerve. If extrasystoles occur due to discontinuous stimulus formation vagal stimulation inhibits them.

Summary. Stretching of the auricular muscle fibers during a tachycardia induced by aconitine leads to an increase of rate and to transient auricular fibrillation. Transient auricular fibrillation (or flutter) can be elicited by stretching during a period of 15-20 minutes after the aconitine arrhythmia has subsided and sinus rhythm prevails.

Because there is much evidence that stretching changes impulse formation and not impulse conduction these results are believed to bring further evidence against the circus movement hypothesis.

The experiments offer an explanation for the appearance of paroxysmal fibrillation induced by physical exertion.

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17042

Cortical Projection of Proprioception in the Cat and Monkey.*

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In spite of the abundant evidence of the importance of proprioception for the regulation of movements in general and those elicited by stimulation of the motor cortex in particular[1-3] little is known about the action of proprioceptive impulses on the cortex.†

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

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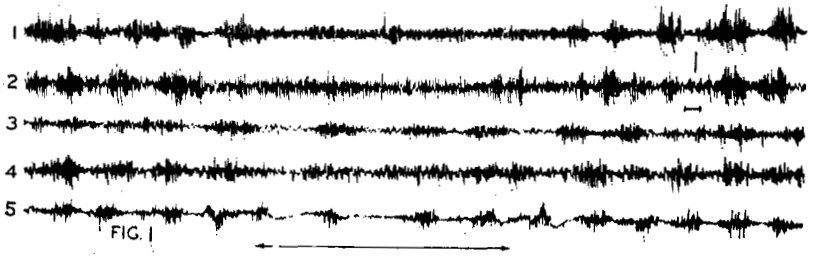
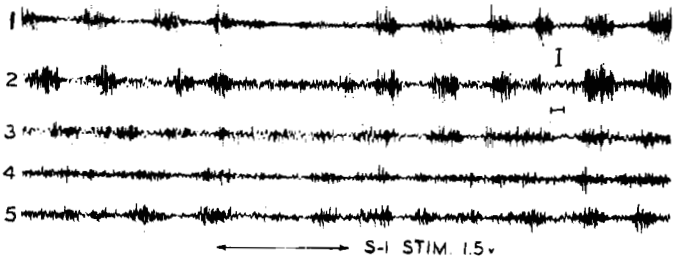


FIG. 1



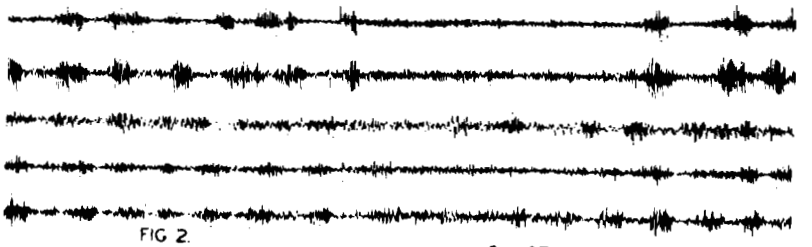


FIG 2.

S-1 STIM. 1.9v

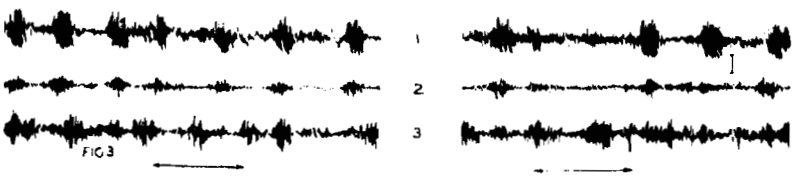
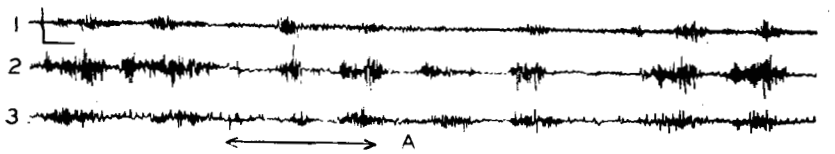


FIG 3



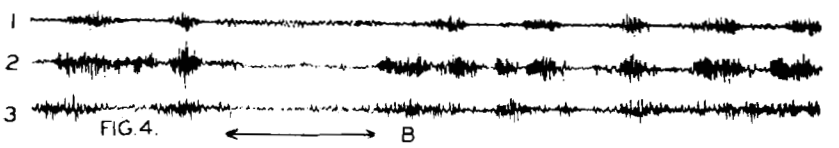


FIG. 4.

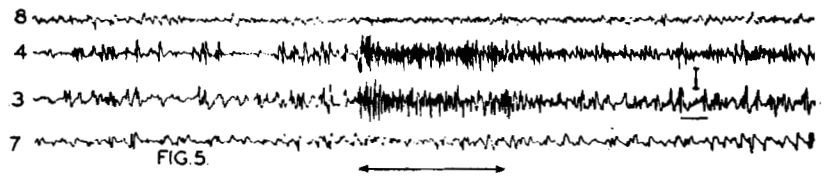


FIG. 5.

FIG. 1. Effect of passive extension of r. hindleg (knee extended to 160°, ankle to plantar flexion of 140°, duration of movement indicated by arrow) on the corticogram of the cat. 1, r, sensorimotor area; 2, l. sensorimotor area; 3, l. temporal region; 4, l. occipital region; 5, l. parietal region. Calibration in Fig. 1 to 5 300 microvolts and one second.

FIG. 2. Effect of stimulation of peripheral end of r. first sacral ventral spinal root (S_1) with condenser discharges (1.5 volts, 90 per second, upper part of figure; 1.9 volts, 90 per second, lower part of figure) on the E.C.G. of the cat. No. 1 to 5 as in Fig. 1. Duration of stimulation indicated by arrow.

FIG. 3. Effect of stimulation of r. S_1 (1.5 volts, 90 per second) on the E.C.G. of the cat before and after reinforcement by fixation of stimulated extremity in extension. 1, l. motor cortex, 2, l. sensory cortex (gyrus proreus), 3, l. auditory area. Left figure without fixation; right figure, knee fixated at 150° and ankle at 130°.

FIG. 4. Effect of stimulation of r. S_1 (1.5 volts, 90 per second) on left E.C.G. of the cat. 1, sensorimotor area, 2, parietal cortex, 3, occipital cortex. R. tibialis anterior and gastrocnemius muscles tenotomized. In experiment A tendons without tension. In experiment B tendons under tension by application of 225 g weight to each tendon.

FIG. 5. Effect of stimulation of r. S_1 (1.0 volts, 90 per second) on contralateral cortex of the monkey. The numbers 8, 4, 3, 7 indicate the eye field, motor area, postcentral gyrus, and parietal lobe respectively.

That the motor cortex is involved is suggested by Bard's[5] observation that the contralateral hopping reaction is abolished in the monkey by ablation of the motor cortex. If the postcentral gyrus alone is removed this reaction is lost temporarily (Peele).[6] That the precentral gyrus plays a role in proprioception is further indicated by the fact that stimulation of posterior roots elicits, in addition to potentials in the postcentral gyrus, also changes in area 4 which are not of tactile origin (Woolsey, Chang and Bard).[7] While the present work was in progress Dawson[8] showed by means of EEG records that stretching a contralateral muscle elicited a myoclonic seizure accompanied by distinct potential changes over the central part of the skull corresponding to the contralateral area 4.

It is the purpose of this paper to report experiments which demonstrate the cortical projection of proprioceptive impulses in cat and monkey.

Method and material. The experiments were performed on 35 cats and 8 monkeys (Macaque) anesthetized with 0.45 cc dial-urethane per kilo i.p. The exposure of brain and spinal cord followed standard procedures. Cortical potentials were recorded with an Offner inkwriter after proper amplification as in previous experiments. For eliciting proprioceptive impulses several methods were used: 1. gentle passive movements of one hindleg; 2. stimulation of the peripheral end of a motor root, usually S_1 as previously described by Cooper and Creed.[9] A shielded electrode of special design was used which permitted repetition of this experiment over periods as long as 24 hours; 3. stimulation of the central end of a muscle nerve with threshold currents.

Results. I. The effect of proprioceptive impulses on the cortex of the cat, a. Effect of proprioceptive impulses induced by passive movements. Passive flexion and extension studied in 5 cats were equally effective in causing an excitation of the cortex which was

† The role of proprioception in cortically induced convulsions has been studied by Gellhorn, Hyde, and Gay.[4]

[4] Gellhorn, E., Hyde, J., and Gay, J., *Arch. Internat. Pharmacodyn.*, 1949.

[5] Bard, P., *Harvey Lectures*, 1938, **33**, 143.

[6] Peele, T. L., *J. Neurophysiol.*, 1944, **7**, 269.

[7] Woolsey, C. N., Chang, H. T., and Bard, P., *Fed. Proc.*, 1947, **6**, 230.

[8] Dawson, G. D., *J. Neurol. Neurosurgery Psychiat.*, 1947, **10**, 141.

[9] Cooper, S., and Creed, R. S., *J. Physiol.*, 1927, **62**, 273, and **64**, 199.

characterized by the disappearance of "Dial" potentials and/or an increase in the frequency and amplitude of the background potentials. Frequently the cortical effect appeared only on the contralateral sensori-motor areas; sometimes (Fig. 1) the effect was present in both sensorimotor cortices but greater on the contralateral side. Temporal, parietal and occipital areas were consistently negative. Passive movements were repeated at intervals of more than three minutes and it was observed that the excitatory effect on the cortex gradually diminished with each successive movement. After 4 or 5 tests the changes in cortical potentials were no longer obtained.

b. *Proprioceptive impulses induced by ventral spinal root stimulation.* Stimulation of the peripheral end of S_1 which produced a strong contraction of both flexor and extensor muscles of the hindleg with condenser discharges of 1.0 to 1.5 volts (90 per second) was used in 11 cats. Electrocorticograms recorded during such stimulation showed an excitation which was greater on the side contralateral to the limb stimulated and most marked in the sensori-motor area. A stronger stimulus was required to elicit both a muscular contraction and a cortical effect than to evoke a muscular contraction alone.

Fig. 2 shows the effect of 2 different intensities of stimulation applied to S_1. The weaker stimulus produced cortical changes confined to the period of stimulation whereas the stronger stimulus greatly prolonged the excitatory effect. The "Dial" potentials disappeared in the sensori-motor areas and were unaltered in the other projection areas on stimulation of S_1 with 1.5 V, but in response to stimulation with 1.9 V some slight excitation was present outside the sensori-motor area although to a much lesser degree than in the latter. The greater amplitude of the potentials in the contralateral than in the ipsilateral sensori-motor area in both tests suggests more recruitment of neurons in the contralateral cortex.

Since it was pointed out in previous investigations that proprioceptive impulses modify cortically induced movements more effectively when the muscle contractions occur under isometric conditions the experiments with stimulation of S_1 were repeated under conditions of fixation of joints. By properly adjusting its intensity a stimulus was used which although inducing a contraction of the muscles failed to alter cortical potentials. If, however, the same stimulus was repeated while the leg was fixated in extension the "Dial" potentials disappeared in the contralateral cortex (Fig. 3). Similar results were seen with fixation in flexion.

These experiments showed that proprioceptive impulses originating in nearly isometrically contracting muscles were particularly effective in altering cortical potentials. As an illustration of primary involvement of muscle tension Fig. 4 shows that S_1 stimulation of tenotomized muscles was ineffective on the cortex while the same stimulus applied when the muscles were kept stretched with a load elicited marked potential changes in the contralateral cortex.

c. *Cortical projection area of proprioception in the cat.* The experiments reported in the preceding paragraphs have already indicated that proprioceptive impulses are projected to the cerebral cortex and involve primarily the contralateral sensori-motor cortex. Even in the recordings in which several diverse areas of the cortex were excited, the potential changes decreased with increasing distance from the sensori-motor cortex. These findings led to a more detailed study of the projection of proprioception to the cerebral cortex (11 cats) based on stimulation of S_1.

A composite map of the contralateral projection area of proprioception is shown in Fig. 6. Each point on the map was verified in 2 or more animals. The principal area excited by proprioceptive discharges was the contralateral sensori-motor cortex while temporal, parietal and occipital areas were unchanged. A few points believed to be located in areas 2s and 19s appeared to be excited.

In contradistinction to this group it was seen in several animals (degree of anesthesia ?) that the cortical response to proprio-

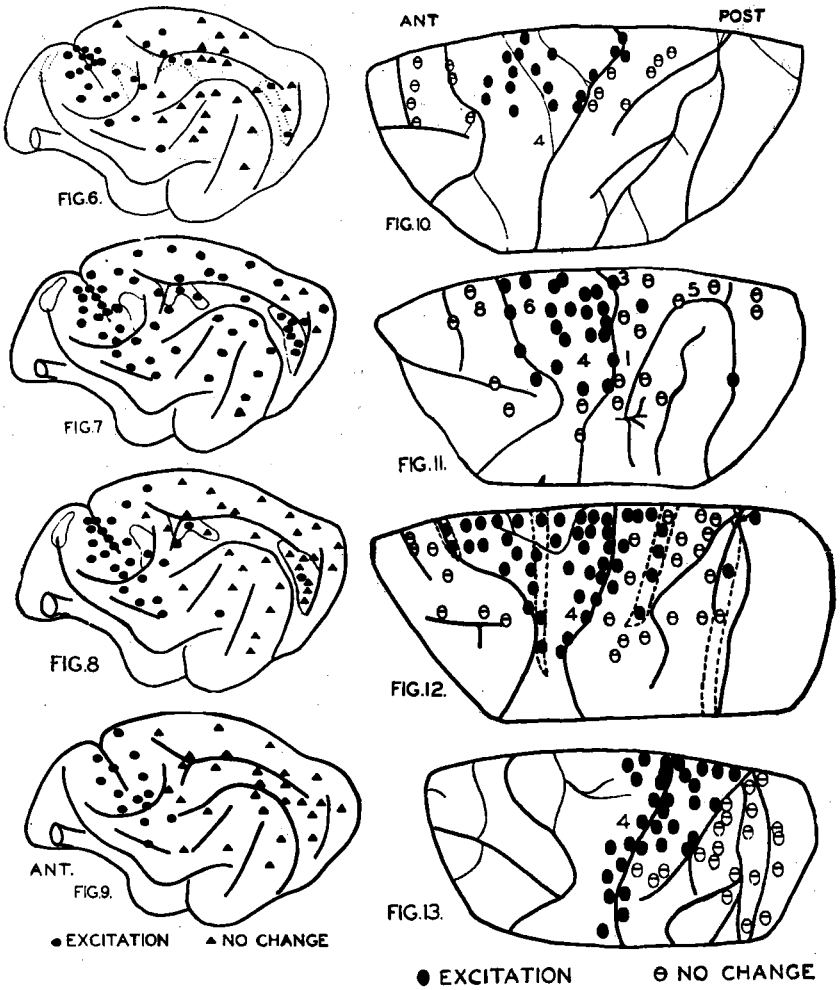


FIG. 6. Projection area of proprioception in the contralateral cerebral cortex of the cat determined by ventral spinal root stimulation or passive movements of extremities in several animals. Oval symbols represent points of excitation, triangles indicate no change. Each point was verified in more than one experiment and more than one animal.

FIG. 7 and 8. Area of projection of proprioception following contralateral stimulation of S_1 in the same cat. In Fig. 7 all points showing disappearance of "Dial" potentials on stimulation are marked positive whereas in Fig. 8 only those points showing in addition increased background activity are indicated by oval symbols.

FIG. 9. Projection of proprioception in the cerebral cortex of the cat determined by stimulation of a nerve from the contralateral gastrocnemius muscle.

FIG. 10 to 13. Projection area of proprioception in the contralateral cerebral cortex of four monkeys determined by ventral spinal root stimulation (S_1).

ception tended to be a diffuse phenomenon. Thus, in the experiment shown in Fig. 7 the entire cortex was responsive except the occipital and temporal poles. However, a careful examination of the records showed that the degree of excitation was quite different in different parts of the cortex. If a distinction is made between reactions consisting of temporary disappearance of dial potentials only and those responses in which in addition the background potentials were markedly increased, it can be shown that the sensorimotor cortex is more strongly affected. In Fig. 8 a map of the same cortex is represented as

in Fig. 7 but only those points are marked as positive which showed increased background activity in addition to the loss of "Dial" potentials (asynchrony plus recruitment. cf. Gellhorn).[10] This figure shows a clear relation of proprioceptive impulses to the sensori-motor cortex. Again two points believed to be located in areas 2s and 19s were positive although surrounded by an unresponsive region.

Proprioceptive projection was also studied by stimulating the central end of the nerve supplying the medial head of the gastrocnemius muscle. At 1.0V a small ipsilateral reflex contraction occurred but no change in cortical potentials. Stimuli of 1.5 or 1.9V resulted in excitation of the contralateral sensori-motor cortex whereas 2.3V caused bilateral excitation of all cortical areas. For mapping purposes the weaker stimulus (1.5V) was used. The effect (Fig. 9) resembled the maps shown in Fig. 6 and 8.

II. *The effect of proprioceptive impulses on the cortex of the monkey.* a. *Proprioceptive impulses induced by ventral spinal root stimulation.* The effects of ventral spinal root stimulation on the cerebral cortex of the monkey closely resemble those seen in the cat. When a subthreshold stimulus (contraction of limb muscles without cortical change) was employed, fixation of the limb in a position of flexion or extension was usually successful in augmenting proprioceptive impulses which led to an excitation of the cortex. The most marked excitation was observed in the contralateral cortex and consisted of a great increase in frequency and amplitude of the potentials in area 4 and the closely adjacent part of the postcentral gyrus while the potentials in area 8 and 7 remain unchanged (Fig. 5). The degree of specificity of the cortical projection area is also indicated by the fact that the various parts of area 4 were unequally affected by stimulation of S_1, the change being the greatest in the medial (hindleg) area and progressively diminishing with increasing laterality.

Experiments on passive flexion or extension showed slight effects on cortical potentials restricted to the contralateral area 4.

b. *Cortical projection area of proprioception in the monkey.* The projection pattern of proprioception was much more specific in the monkey than in the cat. Excitation of the cortex induced by either passive movements, spinal root (S_1) or afferent muscle nerve stimulation was confined to the precentral motor area (area 4 and 6) and to a much lesser extent to adjacent portions of the postcentral sensory cortex (Fig. 10 and 11), In two animals (Fig. 12 and 13) the excitation extended somewhat more posteriorly in the postcentral sensory cortex to include areas 2s in one animal and area 2s and 5 in the other animal. Points anterior to area 6 and posterior to area 5 and those located in the central portion of the temporal lobe were consistently negative (no excitation). None of the monkeys showed a widespread excitation of the cortex of the type seen in the cat when the same ventral spinal root was stimulated.

The degree of excitation induced by proprioceptive impulses was greater on the contralateral motor cortex. The excitation of the ipsilateral hindleg area was very slight on stimulation of S_1 and was of the same order of magnitude as that found in the face area of the contralateral cortex.

Discussion. The uniform results obtained with passive movements, stimulation of the peripheral end of a sectioned motor root, and of the low threshold fibers of a muscle nerve known to consist of proprioceptive nerves indicate that proprioceptive nerve fibers were stimulated. Tactile receptors are not involved since in "Dial" anesthesia methods used in this paper failed to show any changes in the corticogram on tactile stimulation. Neither do nociceptive impulses play any role in these results since the effect of the above procedures is regularly eliminated by ipsilateral hemisection of the spinal cord‡ whereas the widespread cortical action of stimulation of a posterior root persists after this operation.

The effect of proprioceptive impulses on the cortex of the cat was found to be more diffuse than in the monkey. Whether this

[10] Gellhorn, E., and Ballin, H. M., *Am. J. Physiol.*, 1946, **146**, 630.

indicates a species difference or rather a different reaction due to different degrees of anesthesia is impossible to decide at present. The diffuse action noted on the cortex of the cat seems to be akin to a general awakening effect. This is interesting inasmuch as the relation of proprioceptive impulses to the state of wakefulness is well established (Kleitman).[11]

It is worthy of note that in some instances proprioceptive impulses elicited an excitation of cortical suppressor areas. Dick, Bosma and Gellhorn[12] showed recently that stretching of contractured muscles caused a temporary suppression of cortical potentials and of the responsiveness of the motor cortex to electrical stimulation.

Previous experiments have established the fact that cortically induced movements are greatly modified by proprioceptive impulses particularly if the latter are intensified by fixation of joints so that muscle contractions proceed with minimal shortening. The present work gives evidence that proprioceptive impulses alter cortical activity and that the core of this effect resides in the contralateral motor cortex. These impulses are obviously necessary for the performance of cortical proprioceptive reflexes such as the hopping reaction (Bard). However, whether the cortical projection of proprioceptive impulses is responsible for the modification of cortically induced movements is uncertain. Unpublished experiments by Loofbourrow and Gellhorn have shown that spinal nociceptive reflexes are altered in a very similar manner under conditions of proprioceptive reinforcement. Even the myotatic reflex excited by stretch in a given muscle is not restricted to this muscle but extends its effect to other muscles which appear in a similar functional grouping as seen under conditions of stimulation of the motor cortex.[13] It is therefore quite probable that proprioceptive impulses modify cortically induced activity by altering the reactivity of spinal and not that of cortical neurons and this interpretation may be valid for the previously reported effects of nociceptive impulses on cortically induced movements (Gellhorn and Thompson).[14]

It is believed that the most important cortical function of proprioceptive impulses has to do with the initiation of voluntary movements. The fact that a deafferented extremity becomes useless in higher animals although no essential change occurs in the effect of electrical stimulation of the motor cortex (Sherrington,[15,16] Hyde and Gellhorn[3]) suggests an action of proprioceptive impulses on the motor cortex. The experiments presented in this paper have provided this evidence.

Summary. The effect of proprioceptive impulses on the corticogram was studied in cat and rhesus monkey by 1. passive flexion and extension of an extremity, 2. stimulation of the peripheral end of a ventral spinal root with condenser discharges, 3. stimulation of the central end of a muscle nerve. Excitation was indicated by disappearance of "Dial" potentials and/or increase in amplitude and frequency of background potentials. That tension receptors were primarily involved was shown by the fact that a stimulus of S_1, subthreshold as far as the cortical effect was concerned, became effective if the muscles contracted isometrically or under load.

The principal area of the cortex which was excited by proprioceptive impulses was the sensori-motor area in the cat and the precentral motor cortex in the monkey. In several cats the excitation induced by proprioception was spread diffusely throughout the contralateral hemisphere except for the extreme poles, but the excitation was greatest in the

‡ Unpublished observations.

[11] Kleitman, N., Sleep and Wakefulness, Chicago, 1939.

[12] Dick, C., Bosma, J., and Gellhorn, E., *Arch. Internat. Pharmacodyn.*, 1949.

[13] Loofbourrow, G. N., and Gellhorn, E., *Am. J. Physiol.*, 1948, **154**, 433.

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

[15] Mott, F. W., and Sherrington, C. S., *Proc. Roy. Soc.*, 1895, **57**, 481.

[16] Sherrington, C. S., *Philos. Trans.*, 1893, **184** B, 641.

sensori-motor area. In the monkey the cortical effect was more restricted and appeared in the precentral motor cortex (area 4 and 6) and, to a lesser extent, in the adjacent part of the postcentral sensory cortex. When proprioceptive impulses were elicited in a hindleg of a monkey the area of greatest change of potentials was in a hindleg point of the contralateral motor cortex. Lesser degrees of excitation were seen in arm and face area and also in the ipsilateral leg area.

It is suggested that proprioceptive impulses to area 4 are involved in voluntary movements. Their absence accounts for the loss of voluntary movements of the deafferented limb in the monkey although no change occurs in its responsiveness to electrical stimulation of the motor cortex.

17043 P

Effect of Curare on Autonomic Reflexes.*

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The current trend to utilize curare for muscular relaxation during surgical anesthesia has led to observations disclosing a depressor effect of curare for certain autonomic reflexes.

a. Celiac plexus reflex. Pressure stimulation at the celiac plexus during surgical manipulation may result in reflexogenic changes consisting of a fall in the systolic blood pressure, a marked diminution in pulse pressure, little or no change in pulse rate, and rigidity of abdominal muscles.[1,2] Administration of therapeutic doses of d-tubocurarine to 12 patients who presented such a syndrome during upper abdominal surgery, not only provided adequate muscular relaxation but also resulted in a return in the arterial blood pressure and in the pulse pressure to normal which were then sustained.

Experimental investigations in a series of 8 dogs corroborated the clinical observations. The arterial hypotension with marked decrease in pulse pressure produced by compression of the celiac ganglion were not obtained after the intravenous administration of d-tubocurarine (2 units per kg).

b. Carotid sinus reflex. The results observed following the intravenous injection of d-tubocurarine during carotid sinus stimulation showed similar effects.[3]

Two patients having radical neck dissection manifested characteristic carotid sinus reflex activity with severe arterial hypotension and significant bradycardia. The intravenous administration of 40 units of d-tubocurarine resulted in a restitution of the arterial blood pressure and the pulse rate within 3 minutes.

Experimental investigations in a series of 8 dogs showed similar consistent effects. Upon pulling a tape applied about the carotid bulb during pentothal sodium anesthesia there followed arterial hypotension and bradycardia. After the intravenous administration of d-tubocurarine (2 units per kg) repeated similar stimulation of the carotid sinus failed to elicit any cardiocirculatory disturbance.

* Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

1 Burstein, C. L., and Rovenstine, E. A., *Arch. Surg.*, 1939, **35**, 599.

2 Burstein, C. L., and Rovenstine, E. A., *Curr. Res. Anesth. and Analg.*, 1938, **17**, 134.

3 Heymans, C., Bouckaret, J. J., and Regniers, P., Le sinus Carotidien, G. Doin et Cie, Paris, 1933.