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Effect of Ablation of Sensory Cortex upon the Threshold to Pain Reaction.*

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Head,[1] elaborating upon the work of Dejerine, located the sensory level for pain perception in the thalamus. Since then there has been accumulated a vast amount of clinical material stressing the importance of this sensory level for pain sensibility. It has also been shown that 2 other forms of sensory intensity discrimination are not permanently diminished by ablation of relevant sensory cortical areas. Lashley,[2] in rats, and Marquis and Hilgard,[3] in monkeys, found no significant loss of brightness discrimination after ablation of the occipital cortex. Ruch,[4] found no loss in weight discrimination after ablation of the sensory cortex in monkeys. The development of a quantitative, sensitive experiment capable of differentiating the rôle of cortex and thalamus in establishing the threshold to pain reaction was therefore considered desirable.

Adult cats, of over 5 pounds, were used. In 5 of these animals, one hind leg cortical sensory area, as delimited by Bard and Brooks,[5] was removed by their technic. Marshall, Woolsey and Bard[6] have shown by action currents that the tactile sensibility of the entire body, excluding the face, is represented contralaterally in the cortex. All of these 5 animals showed a permanent loss of the dorsal placing reaction of Bard only on the contralateral hind leg, without motor disturbances. The dorsal placing reactions were present on the 3 normal legs. In one animal, No. 8, the sensory and motor area of the right hind leg was destroyed, which gave permanent loss of the dorsal placing reaction on both right legs, and a transient extensor paralysis and walking defect on the right hind leg. In one animal, No. 12, the entire right cortex back of the motor area to the occipital

* Aided by a grant from the Graduate School of the University of Illinois.

1 Head, H., and Holmes, C., *Brain*, 1911, **34**, 107.

2 Lashley, K. S., *J. Comp. Neur.*, 1926, **41**, 1.

3 Marquis, D. C., and Hilgard, E. R., *Brain*, 1937, **60**, 1.

4 Ruch, T. C., *Assn. for Research in Nerv. and Ment. Diseases Publications*, 1935, **15**, 289.

5 Bard, Phillip, and Brooks, Chandler M., *Assn. for Research in Nerv. and Ment. Diseases Publications*, 1934, **13**, 107.

6 Marshall, W. G., Woolsey, C. N., and Bard, Phillip, *Science*, 1937, **85**, 388.

cortex was electro-coagulated. Placing reactions were absent on both left legs, but present on both right legs.

Experiments were begun 3 weeks after the operation. The animals were placed in a box with a head holder which kept the head fixed, but allowed free observation of the eyes. After a variable period of training, lasting from 3 to 25 days, the animals would remain quiet throughout the experiment. Thus, no anesthesia was necessary. The middle toe pads were stimulated by unipolar electrodes, connected to an inductorium with the hammer silenced. All sources of conditioning were avoided. Readings were taken one minute apart, and the alternate thresholds required to elicit pain reaction from stimulation of both normal and cortically ablated hind legs were determined.

The pain reaction chosen as the indicator was the reflex dilation of the pupil. This dilation occurs solely by an inhibition of the constrictor tonus mediated through the Edinger-Westphal nucleus. Cutting the oculomotor nerve abolishes the reaction. Absence or presence of the cervical sympathetic does not alter the threshold of the reaction. Deep narcosis or atropine abolishes the reaction. As a control 2 cats were prepared with unilateral vago-sympathectomy. Both eyes responded with dilation at the same threshold. That this reaction is exclusively an inhibition was first clearly stated by Bechterew,[8] elaborated by Braunstein,[9] and reaffirmed by Bain, Irving and McSwiney.[10] Further, Ury and Gellhorn, in unpublished work, confirm these previous investigators.

The animals with cortical lesions were placed in the box, and the head illuminated by a strong, constant light. The eyes were observed through a low-power microscope, fitted with a graduated scale, on which one division equalled 1 mm. of pupillary diameter. A dilation of one division was considered subthreshold, and a dilation of 2 divisions as the threshold reaction. This reaction occurs within the second of stimulation, and is reversible in from one to 2 seconds. The pupillary reaction is the constant and unfailing precursor of more violent pain reactions, such as moving or crying. A shortening of the coil distance 0.5 cm. from the point which gave the threshold pupillary reaction gave these stronger, more generalized reactions. Both eyes react simultaneously and to the same degree, irrespective

[7] Dusser, de Barenne, *Assn. for Research in Nerv. and Ment. Diseases Publications*, 1935, **15**, 265.

[8] Bechterew, W., *Pfluger's Arch.*, 1883, **31**, 60.

[9] Braunstein, *Zur Lehre von der Innervation der Pupillen Bewegung*, Wiesbaden, 1894.

[10] Bain, W. A., Irving, J. T., and McSwiney, B. A., *J. Physiol.*, 1935, **84**, 323.

of the leg stimulated. Under these experimental conditions the dilation of the pupil in response to an afferent stimulus is a constant, sensitive indicator of a central process associated with pain. It is caused by a central inhibition, and is uncomplicated by any variable factors in the periphery.

Results are best expressed by graphs. Twenty-six experiments were done on 5 animals which had unilateral ablation of one hind leg sensory zone. In 23 of these experiments no essential difference in threshold was noted between the normal and ablated side. In 2

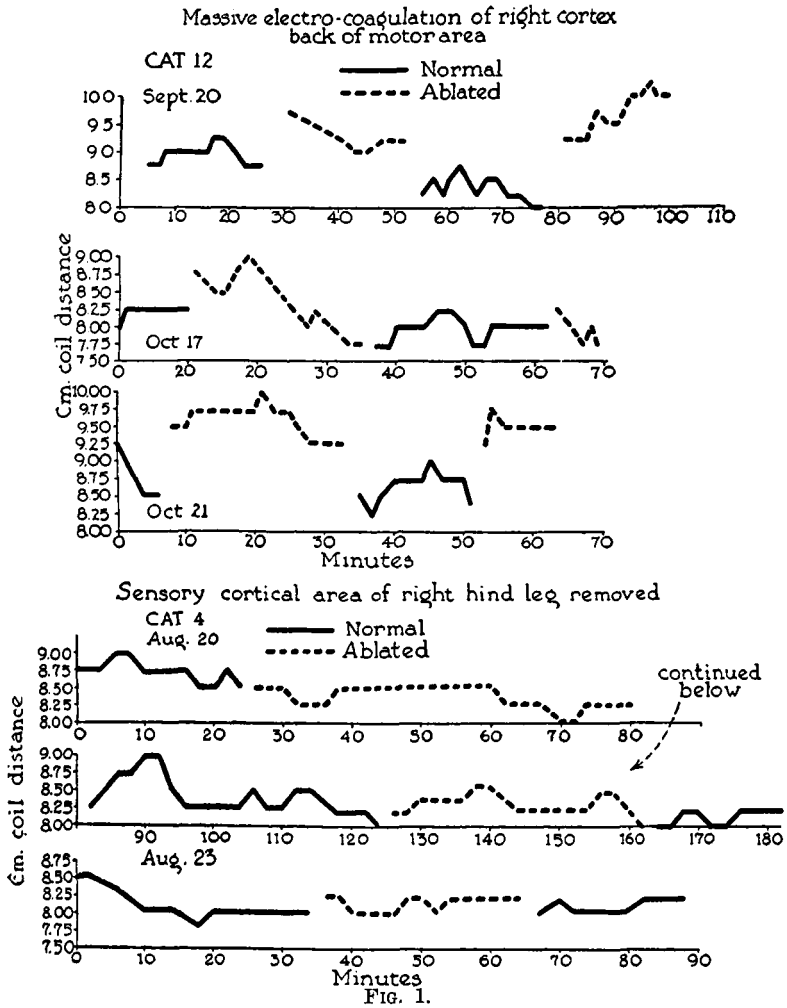

FIG. 1.

The graphs show the coil distance necessary to obtain the threshold reaction. The ordinate is coil distance in cm., the abscissa is time in minutes.

experiments the ablated side was slightly more sensitive, ½ cm. on the coil and in one experiment the normal side was slightly more sensitive. Twelve experiments were done on Animal No. 8, with sensori-motor ablation. In 3 experiments the normal side was slightly more sensitive, ½ cm. on coil, and in one experiment the ablated side was more sensitive to the same degree. Nine experiments were done on Cat No. 12, which had massive electro-coagulation of the right cortex. In 7 of these experiments the animal showed a greater sensitivity when the leg projected to the ablated side was stimulated. This increased sensitivity showed a gradual decrease during the 4 months this animal has been studied, during which time the normal side retained a comparatively constant level of response. Whether this is an individual response or a general tendency of such preparations is to be further investigated. Further experiments involving conditioned reflexes, frontal lobe ablations, and histological study of the brain have been initiated.

Conclusion. Ablation of the sensory cortex alone, or of the sensory and motor cortex, does not raise the threshold to pain reaction. In one animal massive unilateral ablation of the cortex made the animal more sensitive to painful stimuli applied to a body surface projected upon the ablated cortex.

The authors wish to thank the Physiology Department of the College of Medicine for the use of space and of apparatus essential to the performance of these experiments.

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Respiratory Quotient of Diabetic Liver.

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Studies have been published on the metabolism of the liver tissue excised from animals in various nutritive states; on normal diet, or during high fat feeding, as well as of fasted animals. Gemmill and Holmes[1] have reported the respiratory quotients of rats on well-balanced rations to average 0.78, and high fat diet, 0.58. Marsh[2] obtained similar results with fasted rats whose respiratory quotients average from 0.59 to 0.60. Elliott and Baker[3] noted a respiratory

1 Gemmill, C. L., and Holmes, E. G., *Biochem. J.*, 1935, **29**, 338.

2 Marsh, M. E., *J. Nutrit.*, 1937, **13**, 109.

3 Elliott, K. A. C., and Baker, Z., *Biochem. J.*, 1935, **29**, 2433.