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Negative Conditioned Reflexes Versus Absence of Response Elicited from External Inhibition.*

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In connection with a study of the association areas of the cerebral hemispheres which are essential for obtaining correct conditioned differential responses of a foreleg with olfactory, auditory, general cutaneous and optic stimuli, a correct absence of response appeared in some of the early negative tests with normal and operated dogs, which at first was confused with a later well-differentiated negative conditioned reflex.

Clarification of this reflex requires familiarity with the technic used in the general problem, as follows: Flexion of the foreleg is the conditioned response, to be correctly positive it must occur within 7 seconds, to be correctly negative it must be withheld for 7 to 15 seconds, depending on the time of appearance of the positive reflex. To be called correct, conditioned differential responses required at least 95% correctness when the positive and negative stimuli were given in varied order. A positive or negative conditioned reflex was never reinforced except for error, in which case the positive error was punished by electric shock and the negative by whipping. Emphasis therefore was placed on the correctness of the reflexes rather than on fine discriminations between analysers.

Two sets of correct conditioned differential tests were used for each sense, one based on components and the other on rate. For example in one set of auditory tests the positive conditioned stimulus consisted of tapping a bell once per second and the negative consisted of tapping a board once per second. In the other set, a bell was tapped once per second for the positive stimulus and 3 times per second for the negative stimulus.

A correct negative reflex that could be elicited by *external inhibition*[1] is illustrated by the following example, which is but one from many normal dogs in which the first negative conditioned test resulted in absence of response to an auditory, olfactory, or general cutaneous stimulus. After having acquired the positive conditioned reflex perfectly for the bell tapped once per second, this dog failed to flex his foreleg during the first negative conditioned test for tapping a board. A simultaneous thoracic record (Fig. 1, C)[2] disclosed inhibition of respiration, and there was complete inhibition of all movements. The second negative conditioned test also resulted in absence of foreleg responses. These tests, however, were followed by many other negative tests mixed in varied ratios with positive conditioned tests, and all tests resulted in positive responses, with respiration showing as much excitation for the incorrect negative responses as for the correct positive reflexes, in spite of the punishment which followed the errors. Finally the true negative reflexes appeared and both negative and positive reflexes were perfect under all conditions.

The difference between the genuine negative conditioned reflex and the early negative reflex due to external inhibition resulting from the marked contrast of the stimuli was frequently well illustrated during the correct conditioned differential tests with olfactory sense after prefrontal lobectomy, and during the general cutaneous and auditory differential tests after removal of large portions of the association cortex. A typical example from a dog previously trained to make correct conditioned differential responses with 2 sets of auditory analysers, namely, bell and iron cup, and bell tapped once per second and 3 times per second, was tested after prefrontal lobectomy and removal of a large portion of the posterior association cortex from one hemisphere (All projection centers but optic were intact). The conditioned differential reflexes

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[1] Pavlov, I. P., *Conditioned Reflexes*, Trans. C. V. Anrep, 1927.

[2] Allen, W. F., *Am. J. Physiol.*, 1942, **137**, 783.

based on different rates of the bell were tested first, with the result that it required 200 positive tests intermixed with 96 negative tests before any sign of regularity occurred in the correct responses to the negative conditioned stimuli. In the first 8 sessions of testing after the operations practically all of the positive tests were correct and nearly all of the negative tests were positive and incorrect. The greatest number of correct negative tests came during the first test session, when 3 out of 12 were correct, the first, second, and fourth. Had the results of the early negative tests been listed as true negative conditioned reflexes, and only a few tests been made, this dog might have been reported as retaining its ability to make correct differential responses in spite of its extirpated cortex.

Another typical example of an external inhibition reflex may be cited from a dog which had acquired correct conditioned differential responses with all the routine analysers before the operation, but which after prefrontal lobectomy and bilateral removal of large portions of the association cortex (all projection centers except optic were intact) was unable to acquire correct conditioned differential responses with either set of general cutaneous analysers. In some 700 tests after operation practically all of the positive tests were correct and a large proportion of the negative conditioned tests were positive responses and incorrect. There were, however, 1 or 2 correct negative tests during each day's session, and these could be explained as the result of external inhibition since in these tests there was inhibition of respiration and other movements. The entire picture of every daily session of tests after the operations was one of inability of the dog to make correct differential responses.

That these two negative reflexes are really different is indicated by the following observations: (1) The negative reflex from external inhibition occurs in normal dogs long before there are any signs of correct conditioned differential responses. (2) They may appear in dogs after varying amounts of association cortex have been removed, when correct conditioned differential negative reflexes cannot be executed. (3) The external inhibition reflex is more than mere cessation of nervous activity, for respiration is inhibited and a restless animal becomes quiet. This reflex is apparently simpler than the negative conditioned response and may involve fewer neurons.

These early sporadic inhibitory reflexes have not been observed in all our dogs during the process of acquiring correct conditioned differential responses, but when they do occur it is important that they are recognized.

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Development of Cirrhosis in the Liver of Dogs Deprived of Both Pituitary and Thyroid Glands.*

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It was shown recently that the concentration of all lipid constituents (total fatty acids, phospholipids, free and esterified cholesterol) is greatly increased in the blood of the hypophysectomized-thyroidectomized dog.[1] The present report deals with the condition of the livers of such animals.

The livers of 9 dogs were examined at intervals of 70 to 419 days after they had been deprived of both pituitary and thyroid glands. The completeness of hypophysectomy in all dogs was established at necropsy. A fatty infiltration of the liver was observed in 8 of them. The livers of 6 contained abnormal

* Aided by a grant from the Christine Breon Fund for Medical Research.

[1] Entenman, C., Chaikoff, I. L., and Reichert, F. L., *Endocrinology*, 1942, **30**, 802.