

HABITUATION:

A MODEL PHENOMENON FOR THE STUDY OF NEURONAL SUBSTRATES OF BEHAVIOR¹

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The recent habituation literature is reviewed with emphasis on neurophysiological studies. The hindlimb flexion reflex of the acute spinal cat is used as a model system for analysis of the neuronal mechanisms involved in habituation and sensitization (i.e., dishabituation). Habituation of this response is demonstrated to follow the same 9 parametric relations for stimulus and training variables characteristic of behavioral response habituation in the intact organism. Habituation and sensitization appear to be central neural processes and probably do not involve presynaptic or postsynaptic inhibition. It is suggested that they may result from the interaction of neural processes resembling "polysynaptic low-frequency depression," and "facilitatory afterdischarge." "Membrane desensitization" may play a role in long-lasting habituation.

Perhaps the most fundamental problem in physiological psychology is the elucidation of neuronal mechanisms underlying alterations in behavior. This implies prediction of behavioral changes from descriptions in terms of patterns of synaptic interactions among identifiable populations of neurons. Two general strategies in vogue today are (a) correlational studies relating changes in various neuronal responses of the intact organism to changes in behavior (cf. Morrell, 1961), and (b) analytic studies of relatively long-term changes induced in simplified neuronal systems such as the monosynaptic reflex (cf. Eccles, 1964). At present, phenomena measured in the intact or-

ganism cannot be analyzed in terms of neuronal mechanisms. Analytic studies, while utilizing simpler systems, generally deal with changes whose relationships to alterations in the behavior of the intact organism are not always clear.

The solution to this impasse would seem to be a type of relatively long-lasting and nontrivial alteration in behavior as a result of training which has identical characteristics both in the intact organism and in simplified preparations, where some degree of neuronal analysis is possible. There has been a resurgence of interest in recent years in the phenomena of habituation, due in part to studies of neural response habituation (e.g., Hernández-Peón, Jouvét, & Scherrer, 1957; Sharpless & Jasper, 1956). Behavioral response habituation appears to satisfy both the requirements of behavioral significance and occurrence in simplified preparations. A wide variety of responses of the intact organism habituate (Harris, 1943), as

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do reflex responses of the chronic spinal animal (Prosser & Hunter, 1936). Sufficient information has been developed about the neural organization of the spinal cord to permit some degree of analysis of reflex mechanisms (e.g., Eccles, 1964). This paper will discuss recent studies of habituation with emphasis on neurophysiological findings. We will attempt to demonstrate that habituation of the spinal flexion reflex is identical in characteristics to habituation of more complex responses of the intact organism and is at least partially amenable to analysis in terms of neuronal mechanisms. Original data to be reviewed were all obtained using reflex activity of a "model" mammalian system: the acute spinal cat.

DEFINITIONS

Harris (1943), in his careful and comprehensive review of the earlier literature, defined habituation operationally to be "response decrement as a result of repeated stimulation [p. 385]." Humphrey's (1933) earlier definition, although expressed in less-behavioral terms, is substantially the same. Response decrement resulting from very rapid stimulation (e.g., 500/second) which might be due to invasion of the neuronal relative refractory period has different characteristics and is best excluded, as are decrements resulting from trauma, growth, aging, etc. Habituation can usually be distinguished from the latter phenomena because it is reversible: Habituated responses exhibit spontaneous recovery. The only authority to diverge from Harris' characterization of habituation is Thorpe (1956), who regards it as a "relatively *permanent* waning of a response as a result of repeated stimulation [p. 54; italics ours]." It will be seen that the time course for spontaneous recovery of an habituated

response depends on a great many variables; hence distinctions in terms of recovery time would seem somewhat arbitrary. Certainly Harris' definition has gained widespread acceptance. Several authors have suggested a distinction between "short-term" and "long-term" habituation processes (Shapless & Jasper, 1956; Sokolov, 1955).

Two peripheral mechanisms have often been assumed either explicitly or implicitly to account for response decrement: alterations in receptors or in effectors. These may be given more specific operational definitions which permit empirical evaluation. In this paper, a decrease in receptor activity will be called *receptor adaptation*, and a decrease limited to the effector response (including both effector and neuroeffector junction) will be termed *effector fatigue*. Following Harris (1943), response decrements that can be accounted for entirely by these mechanisms will not be considered habituation.

If a common-denominator definition of learning such as "change in behavior under conditions of practice" is adopted, habituation must be included as an aspect of learning. Habituation can be distinguished from many phenomena of learning in that the change in behavior is a decrease in response strength. It is customary, however, to assume that the response exhibiting habituation is itself unlearned (Harris, 1943). James (1890) and Konorski (1948) have proposed a more inclusive term, *plasticity*, to include habituation, conditioning, and other aspects of behavioral change. Our general definition of habituation may also apply to a variety of other terms: adaptation, accommodation, fatigue, inhibition, negative learning, extinction, stimulus satiation, etc. Habituation will be used here to stand for whichever term the reader

prefers. Martin (1964) has recently proposed that such diverse constructs as response habituation, evolutionary adaptation, and photochemical dark adaptation have a common conceptual basis. The utility of this approach is unclear.

PARAMETRIC CHARACTERISTICS OF HABITUATION

The extensive research on behavioral response habituation in the intact vertebrate has demonstrated a number of parametric relations for stimulus and training variables. Although not previously enumerated as such, examples of all of these may be found in the earlier literature for various reflex responses. Some of the more recent observations, particularly those dealing with types of responses not covered in Harris' (1943) review, will be noted in the brief summary that follows.

1. *Given that a particular stimulus elicits a response, repeated applications of the stimulus result in decreased response (habituation). The decrease is usually a negative exponential function of the number of stimulus presentations.*

Examples of response habituation can probably be found in essentially all behavioral studies where a stimulus is regularly presented. In earlier experiments devoted to habituation, per se, parametric characteristics were studied for a variety of responses (cf. Harris, 1943) ranging from postrotatory nystagmus (Griffith, 1920; Wendt, 1951) to startle (Prosser & Hunter, 1936) and galvanic skin response (GSR—Davis, 1934). With the possible exception of the "knee jerk" reflex (Lombard, 1887; Prosser & Hunter, 1936) habituation was a consistent finding, usually exhibiting an exponential course. The recent habituation literature contains many investigations of various responses which can be subsumed under the general heading of response to novel stimulation, ranging in complexity from simple startle through variously defined orienting reflexes to curiosity, stimulus satiation, and play behavior (Berlyne, 1950, 1960; Bindra, 1959; Butler & Harlow, 1954; Davis, Buchwald, & Frankmann, 1955; Dember, 1961; Dykman, Reese, Galbrecht, & Thomasson, 1959; Engen & Lipsitt, 1965; Glanzer, 1953;

Melzak, 1961; Montgomery, 1953; Robinson & Gantt, 1947; Rodgers, Melzak, & Segal, 1963; Scholander, 1960; Sokolov, 1960; Welker, 1956, 1961). Interestingly, if a single novel stimulus is repeated regularly, habituation of approach behavior follows an exponential course (Glanzer, 1953). Unlearned behavior sequences of birds elicited by certain categories of stimuli have also been found to habituate under some conditions (Hinde, 1954; Thorpe, 1956). Finally, much of the extensive research on response decrement or fatigue under conditions of work (Bartley & Chute, 1947; Robinson, 1934; Solomon, 1948) can be considered within the framework of habituation.

2. *If the stimulus is withheld, the response tends to recover over time (spontaneous recovery).*

Spontaneous recovery is reported in most of the studies noted above and has come to be the most common method of demonstrating that a given response decrement is an example of habituation (Harris, 1943). The time course of spontaneous recovery is markedly influenced by many variables and is not necessarily characteristic of a given response. Thus the habituated startle response to sound in the intact rat may recover in 10 minutes (Prosser & Hunter, 1936) or fail to recover in 24 hours,³ depending upon details of testing. Consequently any categorization of types of habituation based solely on recovery time is likely to be somewhat artificial.

3. *If repeated series of habituation training and spontaneous recovery are given, habituation becomes successively more rapid (this might be called potentiation of habituation).*

Humphrey (1933) noted this effect in his studies on turtle leg withdrawal to shell tap. Konorski (1948) describes it for the orienting response, and it has been described in many studies where repeated habituation series were given (e.g., Davis, 1934).

4. *Other things being equal, the more rapid the frequency of stimulation, the more rapid and/or more pronounced is habituation.*

³J. S. Brown, personal communication, 1964.

Numerous examples of this were noted in the earlier reflex studies (Harris, 1943) as well as in more recent work on stimulus satiation and curiosity (Glanzer, 1953; Welker, 1961). The effect occurs in terms of real time course and occurs within certain limits in terms of number of trials as well.

5. *The weaker the stimulus, the more rapid and/or more pronounced is habituation. Strong stimuli may yield no significant habituation.*

This relationship is characteristic of most types of responses ranging from simple reflexes (Harris, 1943) to complex exploratory behavior (Welker, 1961).⁴

6. *The effects of habituation training may proceed beyond the zero or asymptotic response level.*

Additional habituation training given after the response has disappeared or reached a stable habituated level will result in slower recovery. Although relatively few experiments have studied "below-zero" habituation as such (Humphrey, 1933; Prosser & Hunter, 1936; Wendt, 1931), the observations may be viewed as an extension of the relationship between number of stimulus presentations and degree of habituation. Zero response level is of course to some degree dependent upon the particular response measures used.

7. *Habituation of response to a given stimulus exhibits stimulus generalization to other stimuli.*

Coombs (1938) demonstrated generalization of GSR habituation to different types of auditory stimulation, and Porter (1938) demonstrated cross-modal generalization of the habituated GSR for light and tone stimuli. Mowrer (1934) showed some generalization of postrotatory nystagmus habituation in the pigeon. In a recent study, Crampton and Schwam (1961) reported generalization of optic nystagmus habituation in the cat to different degrees of angular acceleration.

⁴ Postrotatory optic nystagmus may be an exception in that under some conditions the degree of habituation is directly related to velocity of rotation (G. Crampton, personal communication, 1964).

8. *Presentation of another (usually strong) stimulus results in recovery of the habituated response (dishabituation).*

This phenomenon appears to be as ubiquitous as habituation itself and is commonly used to demonstrate that habituation has occurred. Pavlov (1927) was perhaps the first to describe this process (i.e., disinhibition) in relation to an extinguished conditioned response (CR), but also applied it to the habituated orienting response. Humphrey (1933) studied dishabituation extensively in lower vertebrates. Essentially all responses of mammals that can be habituated can also be dishabituated (Harris, 1943). It is not always necessary for the dishabitulatory stimulus to be strong. In fact Sokolov (1960) and Voronin and Sokolov (1960) reported that a decrease in the intensity of an auditory stimulus results in dishabituation of the habituated orienting response in humans. Dishabituation, viewed as neutralization of the process of habituation (Humphrey, 1933), has been perhaps the most important method of distinguishing between habituation and "fatigue."

9. *Upon repeated application of the dishabitulatory stimulus, the amount of dishabituation produced habituates (this might be called habituation of dishabituation).*

Most studies of dishabituation (see above) have noted its habituation. Lehner (1941) has done the most careful parametric studies, showing that habituation of dishabituation follows a negative exponential course for the startle response in the rat and the abdominal reflex in man. More recently, Hagbarth and Kugelberg (1958) and Hagbarth and Finer (1963) verified and extended Lehner's findings for the abdominal and leg flexion reflexes in humans. Crampton and Schwam (1961) have shown that dishabituation of postrotatory nystagmus in the cat by auditory or cutaneous stimuli habituates in a similar fashion.

In reviewing the behavioral habituation literature, it is striking to find virtually complete agreement on the parametric characteristics of the phenomenon in such a wide variety of animals and responses. *These nine*

common characteristics may consequently serve as the detailed operational definition of habituation, replacing the more general definition given above. The extent to which any other response decrements satisfy these characteristics will thus determine whether they can be called habituation.

NEUROPHYSIOLOGICAL STUDIES OF HABITUATION

Electroencephalogram (EEG) Arousal

The EEG arousal response—a rapid transition from slower waves to fast low-voltage activity, usually following sudden stimulation—was observed to decrease upon repeated stimulation in early studies both in animals (e.g., Rhineberger & Jasper, 1937) and man (Knott & Henry, 1941). The first investigation of this effect, per se, was the now classic study by Sharpless and Jasper (1956). Using repeated presentations of brief tones they found that cortical EEG arousal of the sleeping cat becomes shorter and finally disappears. After cessation of stimulation, the arousal response exhibited spontaneous recovery over a period of minutes to hours. Although not studied parametrically, examples of all nine relations listed above for behavioral responses are to be found here and in subsequent confirmatory studies (Caspers, Lerche, & Greuter, 1958; Roig & Sommer-Smith, 1959; Segundo, Roig, & Sommer-Smith, 1959). Apelbaum, Silva, Frick, and Segundo (1960) noted a more restricted generalization gradient when using waking cats than Sharpless and Jasper found with sleeping animals. The human “alpha blocking” response has been shown to habituate to tactile, auditory, and visual stimulation (Sokolov, 1960; Voronin & Sokolov, 1960). Cortical EEG arousal also exhibits habituation, spontaneous recovery, and dishabituation when

elicited by electrical stimulation of the mesencephalic reticular formation (Glickman, 1958; Glickman & Feldman, 1961; Roig & Sommer-Smith, 1959). Habituation of electrographic arousal has also been reported for thalamus and reticular formation (Sharpless & Jasper, 1956), hippocampus (Green & Arduini, 1954), and olfactory bulb (Adrian, 1950; Hernández-Peón, Lavin, Alcocer-Cuarón, & Marcelin, 1960).

Sensory Evoked Potentials

A number of investigators have reported habituation of click- or tone-evoked responses in various regions of the central nervous system (CNS) ranging from the cochlear nucleus to the auditory cortex and mesencephalic reticular formation in the waking animal (Galambos, Sheatz, & Vernier, 1956; Gershuni, Kozhevnikov, Maruseva, Avakyan, Radionova, Altman, & Soroko, 1960; Hernández-Peón et al., 1957; Hernández-Peón & Scherrer, 1955; Jouviet & Hernández-Peón, 1957). Worden and Marsh (1963) have emphasized the importance of controlling stimulus intensity, demonstrating statistically reliable changes in response, and conducting other necessary control procedures which were not always observed in the studies listed above. Experiments satisfying all these methodological criteria have not, for the most part, found any consistent or significant evidence of habituation of auditory evoked responses in the waking animal (Huttenlocher, 1960; Marsh, McCarthy, Sheatz, & Galambos, 1961; Sharpless & Jasper, 1956; Worden & Marsh, 1963). However Marsh and Worden (1964) have recently reported decreases in click-evoked response amplitudes from the auditory cortex when the EEG was desynchronized, even in the absence of any consistent response changes at the

cochlear nucleus. In a recent and careful study, Webster, Dunlop, Simons, and Aitkin (1965) reported a rapid initial decrease in the amplitude of sound-burst-evoked responses of the cochlear nucleus that occurred during the first 30 seconds of stimulation, if the sound (20-millisecond duration) was presented 1/second or *faster*. No decreases occurred with slower rates of stimulation. (The experiments described above generally presented stimuli slower than 1/second and examined responses over periods of many minutes or hours.) Auditory evoked responses of the reticular formation do appear to habituate in the sleeping animal (Huttenlocher, 1960). Auditory evoked cortical association responses do not habituate (Shaw & Thompson, 1964); in fact the amplitude of this response increases during the first few presentations of a click (Thompson & Shaw, 1965). Head position in the sound field is a powerful and consistent determiner of evoked-response amplitude (Marsh, Worden, & Hicks, 1962). Contractions of middle-ear muscles have been implicated in some studies of auditory evoked response habituation (Guzmán-Flores, Alcaraz, & Harmony, 1960; Hugelin, Dumont, & Paillas, 1960), but denied by other workers (Altman, 1960; Moushegan, Rupert, Marsh, & Galambos, 1961). Further discussion of methodological problems is given in the careful studies by Marsh et al. (1962) and Worden and Marsh (1963). (See also the discussion by Deutsch, 1962.)

Many reports have noted habituation of evoked responses from various regions of the visual system to repeated flash stimulation (Cavaggioni, Giannelli, & Santibañez, 1959; Hernández-Peón, Guzmán-Flores, Alcaraz, & Fernandez-Guardiola, 1958; Mancia, Meulders, & Santibañez, 1959; Palestini, Davidovich, & Hernández-Peón,

1959). Pupil diameter apparently was not controlled in many of these early studies. When the eye is atropinized and an artificial pupil used, the evidence for visual evoked response habituation is inconsistent. Fernandez-Guardiola, Roldán, Fanjul, and Castells (1961) found no habituation of responses to flash under these conditions recording from the optic tract and lateral geniculate body and inconsistent changes from the visual cortex: Some preparations showed partial decreases, particularly of the later components of the evoked response, and others showed no decreases. Naquet, Regis, Fischer-Williams, and Fernandez-Guardiola (1960) noted that flash-evoked responses of the visual cortex decreased when pupil diameter increased (concomitant with EEG desynchronization), but did not change when an artificial pupil was used. Affanni, Mancia, and Marchiafava (1962) reported no reduction in responses of the visual cortex to a flash repeatedly presented for hours when an artificial pupil was used. On the other hand, Garcia-Austt (1963) reported decreases in scalp averaged evoked responses to flash in humans with artificial pupils, and decreases of averaged visual evoked responses from the rat after removal of the iris. Responses evoked by somatic sensory stimulation have been reported to habituate (Hernández-Peón, 1960; Hernández-Peón, Scherrer, & Velasco, 1956), and to exhibit no habituation (Santibañez, Trouche, & Albe-Fessard, 1963).

Conclusion

The evidence for EEG arousal habituation is clear and consistent; it exhibits essentially all parametric relations characteristic of behavioral response habituation. Studies of evoked responses, on the other hand, permit only one safe generalization at present:

There is as yet no consistent agreement regarding the occurrence of habituation in sensory systems of the waking brain. Where habituation has been reported, it may be the result of decreases in effective stimulus intensity due to alterations in head position, middle-ear muscle contractions, pupillary constriction, etc., or an indirect result of changes in state of EEG arousal. The issue can only be settled by further research.

EFFECTS OF NEURAL LESIONS ON BEHAVIORAL RESPONSE HABITUATION

Although the majority of studies described here were not planned as parametric investigations of the effects of lesions on behavioral response habituation, per se, many were so designed that such effects could be noted. The orienting response exhibits markedly reduced habituation following chronic total decortication in dogs (Konorski, 1948; Lebidinskaia & Rosenthal, 1935) and chronic decerebration in cats (Bard & Macht, 1958). Lesions of auditory cortex in the cat reduce the extent of intersession habituation of orientation to sound (Thompson & Welker, 1963). Activity level of monkeys with Cortical Area 9 lesions exhibits less habituation than that of normal animals (French, 1959; French & Harlow, 1955). Frontal or temporal lesions in monkeys reduce the amount of visual exploration and decrease the extent of habituation in repeated testing sessions (Butler & Harlow, 1954; Symmes, 1959, 1963). Frontal lesions have a comparable effect in the cat (Hagamen, Lance, & Ungewitter, 1959). Damage to frontal cortex decreases the extent of habituation of the heart-rate response to the cold-pressor test in man and the rat (Glaser & Griffin, 1962; Griffin, 1963). Schwartzbaum, Wilson, and Morrissette (1961) report less-rapid habituation to novel

stimuli following bilateral amygdalectomy. Pribram (1963) reports unpublished results by Kimble and Bagshaw showing comparable effects of amygdalectomy on GSR response to novel stimulation and emphasizes the importance of this structure in habituation.

Response alternation or variability in maze behavior can be related to habituation of response to novel stimuli (see below; also Glanzer, 1953; Welker, 1961). Partial cortical lesions in the rat reduce the tendency to vary movement through a simple maze (Krechevsky, 1937a, 1937b, 1937c). Frontal lesions are more effective than parietal or occipital lesions (Morgan & Wood, 1943). Roberts, Dember, and Brodwick (1962) found that bilateral ablation of the hippocampus resulted in less habituation of T-maze responses and less alternation behavior.

Results of these studies, involving various responses and many different neural structures, are in essentially complete agreement. *Brain damage tends to produce a reduction in the extent of behavioral response habituation.* There is some degree of specificity in that damage to structures related to particular responses tends to have a greater effect on habituation. It would seem that habituation may be mediated, at least in part, by whatever neural structures are most involved in a particular response, suggesting that common neuronal mechanisms may be involved.

SPINAL REFLEXES

Sherrington noted a decrement of the digital flexion of the monkey in 1898, but his experiments on the acute spinal dog (1906) were the first to analyze habituation of spinal reflexes in detail. Although he used the term fatigue, he was careful not to imply any necessary meaning other than response decrement by the term. He

found that continuous or repeated mechanical or electrical stimulation of the appropriate skin region resulted in a decrement of the scratch reflex and the flexion reflex, the former decreasing more rapidly. Both exhibited spontaneous recovery. Several lines of evidence suggested that both receptor adaptation and muscle fatigue could be ruled out. Indirect evidence from a variety of reflex-interaction studies led Sherrington to conclude that the "final common path," that is, the motor neurons, were not fatigued. Prosser and Hunter (1936) completed a careful and extensive study of habituation and dishabituation of the flexion reflex in the chronic spinal rat, using electrical or mechanical stimulation of the legs, tail, and hindlimb nerves. They demonstrated habituation, spontaneous recovery, and dishabituation by strong extraneous stimulation. Weak stimuli led to more rapid habituation than strong stimuli. In one experiment they showed that no habituation occurred in the knee-jerk reflex of a spinal cat. Lehner (1941) demonstrated that the duration of dishabituation of the flexion reflex in the spinal rat habituated.

In conditioning studies of the acute spinal dog, Shurrager and Culler (1941) and Shurrager and Shurrager (1941) demonstrated habituation of the leg flexion reflex to tail stimulation. More recently, Nesmeianova (1957) has demonstrated habituation, spontaneous recovery, and dishabituation of the scratch reflex and the flexion reflex in chronic spinal dogs. Habituation below zero was marked; the response sometimes required days or weeks to recover after long periods of training. Kozak, McFarlane, and Westerman (1962) have reported similarly long-lasting habituation of flexion and scratch reflexes in the chronic spinal kitten. Habituation of the

scratch reflex has also been reported for the chronic spinal frog (Afelt, 1963). Lethlean (1965) has presented evidence suggesting that the flexion reflex may continue to habituate for many minutes after the stimulus has been withdrawn in the chronic spinal rat. Very recent experiments by Buchwald, Halas, and Schramm (1964, 1965) reported habituation of single-unit discharges of motor neurons recorded from ventral root fibers in the acute spinal cat, and a preliminary summary of our own work has already appeared (Spencer, Thompson, & Neilson, 1964).

REFLEX HABITUATION IN THE ACUTE SPINAL CAT

Studies reviewed above indicated that habituation of the flexion reflex in the acute mammalian spinal preparation appears to exhibit some of the parametric relations characteristic of behavioral response habituation in the intact organism. Since a good deal is known about the synaptic organization of the spinal cord, this preparation was chosen as a model system in which to study detailed characteristics of habituation and the possible neuronal mechanisms involved.

The preparation used in these experiments was the acute unanesthetized decerebrate cat with spinal transection at T-12. Procedures are described in detail in papers (in preparation) devoted to analyses of neuronal mechanisms. Data given here are all in terms of isometric "twitch" contraction strength of the tibialis anterior muscle, a hindlimb flexor participating in the generalized limb flexion reflex to afferent stimulation. Other muscles were also studied to insure generality of observations. The flexion reflex is polysynaptic, at least one interneuron intervening between the incoming afferent fibers and the output motor neurons. Dishabituating stimuli were either electrical or natural, that is, pinch. The basic phenomena of habituation and spontaneous recovery were observed on all of the more than 100 cats studied. Spontaneous recovery was used as the criterion that habituation had occurred rather than response decrement due to deterioration or various artifacts. Although not shown in many of the figures, spontaneous recovery was always obtained following every habituation series.

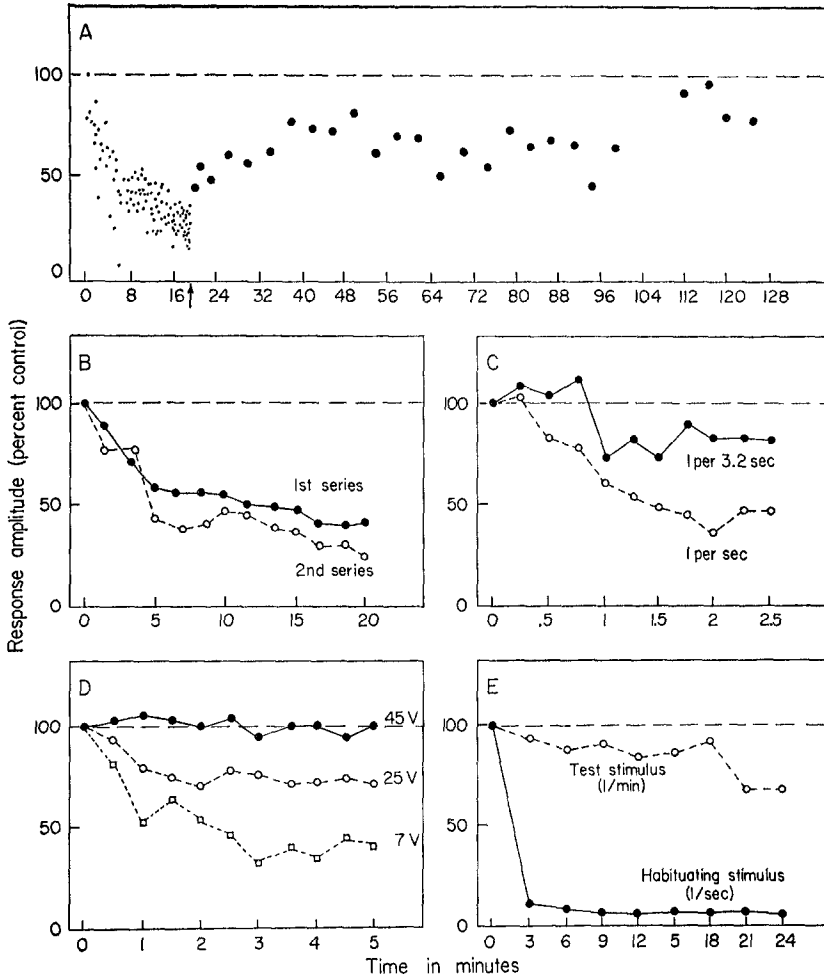


FIG. 1. A: Habituation (zero minutes to arrow) and spontaneous recovery (arrow to 128 minutes) of the hindlimb flexion reflex of the spinal cat in response to repeated skin shocks. (Stimuli were brief trains of shocks—5 in 50 milliseconds—delivered every 10 seconds during habituation and every 3 minutes during spontaneous recovery, except for a 12-minute period of no stimuli at about 100 minutes. In this and all subsequent figures the response measured is tension developed by contraction of the tibialis anterior muscle, expressed as a percentage of mean initial-control response amplitude. B: Effect of repeated-habituation and spontaneous-recovery series on degree of habituation. Response recovered to control level following first habituation series and was then rehabituated—second series. Conditions as in A. Data are averages of 10-trial blocks. C: Effect of stimulus frequency on habituation. Single shocks given 1/3.2 seconds in one habituation series and 1/second in the other to the saphenous nerve. Data are averages of 10-trial blocks. D: Effect of stimulus intensity on habituation. Brief trains of shocks, as in A, were delivered every 10 seconds to the saphenous nerve with spontaneous recovery allowed after each series. Voltages refer to output of stimulator and were attenuated, but in the same ratios, when delivered to the nerve. Data averaged over 3-trial blocks. E: Stimulus generalization of habituation. Single shocks to two separate branches of the saphenous nerve. The habituating stimulus to one branch was given 1/second, and the test stimulus to the other branch was given 1/minute. Data are averages over 3-trial blocks for response to the test stimulus and averages over the same periods of time for response to the habituating stimulus.)

In all experiments, initial-control response amplitudes were first determined by test stimuli delivered no more frequently than 1/minute. Subsequent response amplitudes are plotted in terms of percentage of mean control level. Habituating stimuli were either single shocks (.01-.03-millisecond duration) or brief trains of five such shocks delivered over a 50-millisecond period. Although trains generally gave somewhat more rapid and less variable habituation, the parametric relations of all other variables were comparable for both. Stimuli were delivered to skin or to afferent nerves.

Characteristic habituation and spontaneous recovery of the spinal flexion reflex are shown in Figure 1A. Brief trains of shocks were delivered 1/10 seconds to skin during habituation (0 minutes to arrow) and 1/3 minute during recovery. Individual responses are given to illustrate normal variability. Note the exponential form of habituation and the long and variable time course of spontaneous recovery. Although the time courses of habituation and spontaneous recovery are dependent on the many variables described below, 40 separate series involving a variety of conditions were selected at random from our experiments to determine average values. The mean habituation time was 9.4 minutes (range 1.2-33 minutes), and the mean recovery time was 25.7 minutes (range .5 minute-108 minutes).

The effect of repeated habituation-spontaneous recovery series on habituation is illustrated in Figure 1B. Habituation and recovery conditions are the same as in 1A, and the data shown are averages for 10-trial blocks. The second series exhibits significantly more habituation than the first ($p < .01$; sign test).

Figure 1C shows the effect of stimulus frequency. Here single shocks were delivered either at 1/second or 1/3.2 seconds to the saphenous nerve. Data are averages over 16-second blocks of time. Habituation is significantly greater with the more rapid stimulus ($p < .01$; sign test).

The effect of stimulus intensity on habituation is indicated in Figure 1D. Stimuli were brief trains of shocks to the saphenous nerve every 10 seconds at the indicated voltages. Data are averages of 3-trial blocks. There is no habituation for the 45-volt stimulus, significant habituation for the 25-volt stimulus, and significantly greater habituation for the 7-volt stimulus ($p < .01$ for each comparison; sign test). Thus rate

and degree of habituation are inversely related to stimulus strength.

The development of stimulus generalization of habituation is shown in Figure 1E. Single shocks were delivered to two separate branches of the saphenous nerve. The habituating stimulus was given 1/second, and the generalization test stimulus to the other nerve branch was given 1/minute. Data are averages over 3-trial segments at comparable times for the habituating stimulus. Response to the training stimulus habituated to 10% of control level, and the test-stimulus response decreased to about 60% of control level. Amplitudes of the last 10 habituated, generalized, and control responses all differed significantly from each other (habituated versus control, $t = 18.1$, $df = 18$, $p < .01$; generalized versus control, $t = 2.43$, $df = 18$, $p < .05$; habituated versus generalized, $t = 7.58$, $df = 18$, $p < .01$). Thus there is significant but not complete generalization of habituation from one input channel to another.

The effect of "below-zero" habituation on spontaneous recovery is shown in Figure 2A. Stimuli were brief trains to the sural nerve every 5 seconds. In the recovery curves following habituation to "zero," recovery began when the response had reached a stable level. For the recovery curves following habituation below zero, habituation stimuli were continued for 10-20 minutes after the response had reached a stable level. As seen, spontaneous recovery has a longer time course following below-zero habituation. The habituated levels (i.e., zero recovery time) are comparable for both. The two conditions were alternated 22 times in two separate experiments. The mean spontaneous recovery time following habituation to zero was 2.1 minutes, significantly less than the 7-minute mean recovery time following below-zero habituation ($t = 4.45$, $df = 20$, $p < .01$).

Two examples of dishabituation are shown in Figure 2B. In both cases the response was first habituated to single-shock stimulation of the tibial nerve at 1/3.2 seconds. Weak dishabituation was achieved by increasing the stimulus frequency to 3/second and strong dishabituation by a comparable increase in frequency plus an intensity increase. Habituating stimuli were continued in each series. Data are averages of 8-trial blocks. The weak dishabituating stimulus yielded incomplete recovery, and the strong stimulus resulted in a response of greater than control amplitude. In both cases the response

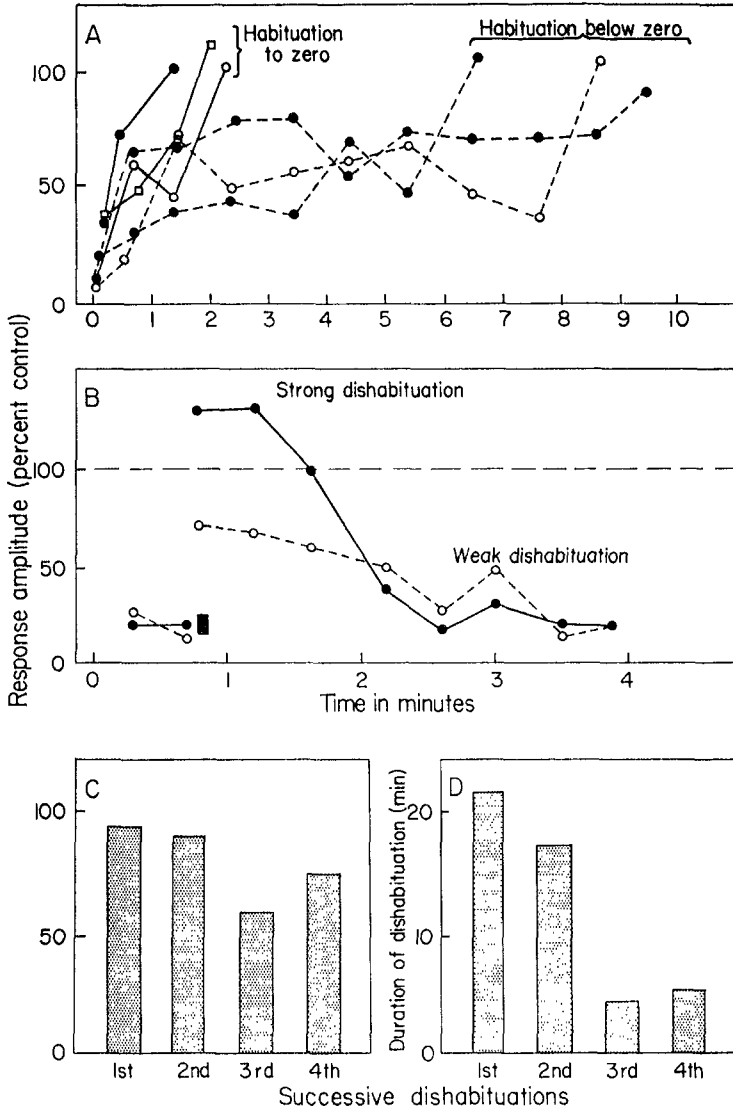


FIG. 2. A: Effect of below-zero habituation on the time course of spontaneous recovery. (Stimuli were brief trains to the sural nerve 1/5 seconds during habituation and 1/minute during the recovery curves shown. Habituation in the to-zero condition was habituation training until the response reached a stable amplitude, and below zero was 10 minutes of additional habituation training after this point had been reached. The to-zero and below-zero conditions were alternated. B: Effects of weak and strong dishabitation on an habituated response. Habituating stimulus was a single shock to the tibial nerve 1/3.2 seconds. Weak dishabitation, bar, was an increase in stimulus frequency to 3/second for 10 seconds, and strong dishabitation was an increase in both frequency and intensity for 10 seconds. Data are averages of 8-trial blocks. C: Habituation of dishabitation. Bars represent the percentage of increase in response amplitude following successive dishabitations delivered when the response was at a stable habituated level. Habituation conditions as in 1A. Dishabitation was a strong pinch of the digits for 5 seconds. D: Same as 2C only duration of the dishabitation effects are plotted.)

returned to habituated levels in about 4 minutes.

Figures 2C and D indicate habituation of dishabituation. Here four successive dishabituating stimuli were given with recovery allowed after each. The habituating stimulus was a brief train of shocks to skin every 10 seconds. Dishabituation was "natural" in this experiment—strong pinching of the digits. There is a reduction both in duration of dishabituation and in amplitude of dishabituated responses following repeated dishabituation.

The data given above illustrate all nine parametric relations characteristic of response habituation in the intact animal. Consequently the flexion reflex of the acute spinal cat exhibits habituation as genuine as that for any response of the intact animal. The time relations for habituation and spontaneous recovery here are within the range of those for responses of the intact animal. It is perhaps somewhat remarkable that a weak stimulus delivered every few seconds for a few minutes can produce a relatively long-lasting but reversible alteration in the behavior of this very much "simplified" nervous system.

Independence of Habituation and Dishabituation

As noted earlier, dishabituation by extraneous stimulation is customarily believed due to disruption of the habituation process, whatever the latter may be. If this were the case, dishabituation ought not to increase the habituated response above its initial control level. However in Figure 2B a strong dishabitulatory stimulus was seen to increase the response *well above* the control level. This observation suggests an alternative hypothesis, namely that dishabituation is a separate facilitatory process superimposed upon the habituated system and probably many other response systems as well. Several testable deductions may be made from this hypothesis. First, nonhabituated responses ought to exhibit dishabituation as well as habituated responses. Figure 3A shows this to be the case; the nonhabituated control-level response is increased markedly by a dishabitulatory stimulus.

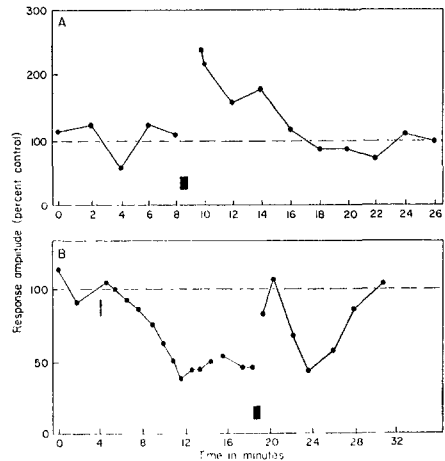


FIG. 3. A: Effect of a strong dishabituating stimulus on an unhabituated (i.e., control-level) response. (Test stimulus was a brief train of shocks to skin every 2 minutes, and dishabituation was a strong shock train delivered elsewhere on the limb for 15 seconds. B: Independence of habituation and dishabituation. Habituation stimulus, arrow to bar, was brief skin-shock train given 1/second and test stimulus given 1/minute. Following the strong, pinch, dishabitulatory stimulus, bar, the habituating stimulus was discontinued and a test stimulus delivered 1/minute. Note that the response dishabituates, then *rehabituates* and spontaneously recovers, even though there is no further habituation training.)

A more crucial deduction concerns the role of the habituating stimulus in the decay of the dishabituation effect. If dishabituation is purely a disruption of habituation, a response which is dishabituated following habituation ought not to rehabituate unless additional habituation stimuli are given. Thus in Figure 2B if the habituating stimulus was turned off after dishabituation, the response should remain at the high dishabituated or control level. Alternatively, if dishabituation is a superimposed facilitatory process having an intrinsic decay time, the dishabituated response should gradually decrease toward the habituated level, *even if no habituation training is given subsequent to dishabituation*. This crucial test of the two alternative hypotheses is illustrated in Figure 3B. After habituation to brief trains at 1/second (arrow to bar), the response is dishabituated (bar), and the habituating stimulus with-

held and introduced only 1/minute to test response amplitude. As seen, the response amplitude declines (or "rehabituates") almost to the habituated level following dishabituation, *even though it is no longer being habituated*. Subsequently it recovers spontaneously to the control level. This finding has been consistently obtained in more than 20 separate experiments. To demonstrate it clearly, conditions must be such that spontaneous recovery has a long time course relative to dishabituation, otherwise the habituated response will partially recover spontaneously by the time dishabituation effects are dissipated. Since dishabituation is not a disruption of habituation, but rather a separate process having all the characteristics of response sensitization (Hilgard & Marquis, 1940), it will hereafter be termed *sensitization*.

Although the independence of habituation and sensitization has not previously been demonstrated as such, several investigators have suggested the possibility. Humphrey (1933), in his studies of habituation in the snail and turtle, noted that a strong dishabituation stimulus caused a response of greater amplitude than prehabituated control responses and would also increase control-level responses prior to habituation. His comment deserves quoting: "These results at once suggest . . . that what has been termed 'dishabituation' is simply an increase in excitability, which, under conditions not known, may summate with repeated stimulation [p. 143]." Sharpless and Jasper (1956) suggested that dishabituation of habituated EEG arousal was probably a transient superimposed facilitation. Pavlov (1927), it should be noted, used the same paradigm we employed in Figure 3B to demonstrate that the disinhibitory effect of an extraneous stimulus on a previously extinguished CR was also transient and had the same decay time whether or not the unreinforced conditioned stimulus (CS) was repeatedly applied.

Sensitization thus emerges as a separate and significant process in its own right. A strong stimulus of very short duration can cause an increase in the excitability of the spinal cord lasting for many minutes. Since sensitization is independent of habituation, at least for the spinal flexion reflex, parametric relations Numbers 8 and 9 are not really relevant to habituation as such,

but rather describe a separate process. In maintaining the comparability of habituation characteristics for responses of the spinal cord and the intact animal, we are forced to the prediction that the independence of habituation and sensitization will also hold for responses of the intact animal. Future research will determine the extent to which this is true. The habituation of sensitization (characteristic Number 9), incidentally, now becomes simply an additional example of habituation, the response being increased excitability of spinal reflexes by the sensitizing stimulus.

Neuronal Mechanisms of Habituation and Sensitization

Analytic studies of possible neuronal mechanisms involved in habituation and sensitization of the spinal flexion reflex are presented elsewhere (Spencer et al., 1964; also papers in preparation). Results of these experiments will be summarized briefly here. Receptor adaptation was ruled out by electrical stimulation of afferent nerves with monitored neurograms indicating no change in input volleys. Effector fatigue was eliminated as a significant variable by recording activity from efferent nerves and ventral roots rather than muscles. The possible role of feedback from muscle activity was eliminated by nerve and root section and by drug paralysis of neuromuscular junctions, including those between gamma motor neurons and intrafusal muscle fibers. These results indicate that habituation and sensitization occur within the spinal cord. In numerous experiments testing possible habituation of the monosynaptic reflex we have found no evidence of habituation in the sense of progressive decrement in response having a time course comparable to flexion reflex habituation.

The excitability of motor neurons in-

involved in a habituated response can be tested by interposing monosynaptic volleys activating them. In addition, using both ventral-root electrotonus as a population measure, and intracellular microelectrode recording of identified motor-neuron membrane potentials for behavior of neuronal elements, the subliminal responses of motor neurons during habituation and dishabituation were also studied. There was no background alteration in the monosynaptic reflex excitability of motor neurons during habituation, but there was a clear-cut decrease in motor-neuron polysynaptic potentials. Thus whatever processes are responsible for habituation occur prior to motor neurons (i.e., in interneuron pathways) and cannot be due to inhibition acting on the motor neurons. During sensitization there was often, although not invariably, an *increase* in the excitability of motor neurons. These observations further substantiate the behavioral demonstration of the independence of habituation and sensitization.

The possibility that habituation is due solely to altered conduction in afferent terminals of nerve fibers stimulated during training is ruled out by the generalization experiment of Figure 1E. If habituation were due entirely to changes in afferent terminals of the habituated channel, there would be no generalization of habituation to the other channel since completely separate input channels were used. Generalization of habituation did occur, so the decrement must have involved central processes shared by both inputs.

To summarize, it has been proven beyond reasonable doubt that habituation of the spinal flexion reflex is not dependent upon receptor adaptation or effector fatigue and occurs after the afferent input terminals but prior to the output motor neurons in the spinal

cord. Consequently the process of habituation must occur in the course of transmission through interneurons. Prosser and Hunter (1936), incidentally, suggested some time ago that this was probably the case. Sensitization, on the other hand, is reflected by increased excitability of both motor and other neurons. Hypotheses and further evidence concerning the processes responsible for habituation and sensitization are developed below.

THEORETICAL ISSUES—BEHAVIORAL

Extinction

The similarity of habituation and experimental extinction was perhaps first emphasized by Humphrey (1930), although Pavlov (1927) had earlier insisted on the basic comparability of unconditioned and conditioned responses. Humphrey (1930, 1933) noted that close parallels exist between the two processes in terms of spontaneous recovery, below-zero effect, and dishabituation. Konorski (1948), in discussing the general properties of plasticity, notes several other parallels including the effect of stimulus frequency and potentiation of habituation upon repeated testing.

The experimental literature on extinction of conditioned responses actually contains many illustrations of the nine parametric relations listed above for habituation (cf. Brogden, 1951; Hull, 1943; Kimble, 1961; Pavlov, 1927). In fact many of these are among the commonly cited characteristics of experimental extinction. To assert that habituation is really extinction does not of course constitute any kind of explanation for either process. By definition extinction presupposes prior conditioning, and the variables of *training* have a potent influence on the characteristics of extinction. Although unspecified prior conditions of learning

may modify or shape many "reflex" activities of the intact organism, habituation does imply an unlearned response. However the fact that habituation and extinction appear to show similar parametric features does raise the possibility that they may share common underlying mechanisms. Although many different pieces of the nervous system are clearly involved in extinction and habituation of various responses, we would like to suggest (in agreement with Sharpless, 1964) that common neuronal mechanisms exist. Response decrements would then be due to a general property of neuronal activity common to all such systems. At least partial analysis of such neuronal mechanisms seems possible in the spinal animal. Hypothetical neural mechanisms consistent with current knowledge of neurophysiology are developed below.

Stimulus Satiation and Related Constructs

A variety of complex behavioral responses such as spontaneous alternation, exploration, and curiosity have been subsumed under the construct of stimulus satiation (Glanzer, 1953). Glanzer's ingenious theory begins with a five-part postulate describing the properties of stimulus satiation and deduces a number of testable predictions about maze running and exploratory behavior. The majority of such predictions have been verified, particularly where deductions from Hull's postulated reactive inhibition lead to opposite predictions (Dember, 1961; Glanzer, 1953). Glanzer's postulate can be viewed as a *formalized restatement of some of the parametric characteristics of response habituation listed above*. All of Glanzer's deductions may also be made from the earlier established properties of response habituation. His general postulate reads: "Each

moment an organism perceives a stimulus object or stimulus objects, A, there develops a quantity of stimulus satiation to A [p. 259]." We may rephrase it as: Each moment an organism responds to a stimulus object or stimulus objects, A, there develops a quantity of *response habituation* to A. Glanzer's deductions follow equally well from this restatement of stimulus satiation in terms of response habituation.

Glanzer's approach has been categorized as a peripheral rather than a central theory (Dember, 1961; Walker, 1958). The above review of neurophysiological studies indicated that there is as yet no entirely satisfactory or consistent evidence for habituation or decrement of evoked responses in primary sensory systems at any level from receptor to cortex. In consequence it would seem misleading to label as *stimulus satiation* a decremental process that *does not appear to exist at any level of neural activity which can be identified with the immediate responses to sensory activation*. Insofar as behavioral responses are concerned, the formal properties of stimulus satiation and response habituation are the same.

Walker (1958) suggested that the term "action decrement," having central locus, be substituted for concepts like stimulus satiation or reactive inhibition. Although he does not relate it to the literature on behavioral habituation, its properties appear to be the same. Dember (1956, 1961) and Dember and Earle (1957) have developed still another theoretical framework for this category of behavior which they term "stimulus change." The organism seeks to obtain the "ideal" amount of "stimulus complexity." Thus in an alternation experiment, the animal alternates choices not because he is satiated or habituated to

one stimulus, but because the other attracts him more (Dember, 1961). Dember (1956) reported an experiment designed as a critical test of stimulus-satiation versus stimulus-change hypotheses. Rats were given experience in a T maze (one arm white, one black) and then tested with both arms the same. He argued that satiation theory would predict no difference in test-choice behavior, but stimulus change would predict more choices of arm different in experience and test sessions. Dember's results verified his prediction. This argument would seem justified if stimulus satiation is limited *only* to alley brightness. However, if the total response pattern of running, orienting, turning, and response to brightness is considered, then generalization of response habituation will be greater to arm same than arm different. Thus analysis in terms of response habituation would also predict more choices of arm different than arm same. As yet there seems to be no clear way of differentiating experimentally between the alternative hypotheses of "avoiding" or habituating to one stimulus complex versus "approaching" another stimulus complex. It has been suggested (Brown, 1961) that this distinction may be fundamentally untestable. Again, the formal behavioral properties of Dember's and Earle's constructs do not appear to differ greatly from those listed above.

To summarize, the formal behavioral properties of stimulus satiation, action decrement, and search for ideal stimulus complexity appear similar to the properties of response habituation. They may well be indistinguishable at the behavioral level. The earlier and more neutral term, habituation, viewed as response decrement, might better serve the search for central neural correlates.

Reactive Inhibition

The construct of reactive inhibition (I_r), developed by Hull (1943) from Pavlov's (1927) more general concept of "inhibitory state," has been shown to have considerable predictive utility, particularly in experiments relating to work performance (Hull, 1943; Solomon, 1948). It is unquestionably the most carefully and extensively analyzed construct dealing with response decrement.

The parametric characteristics of habituation listed above are consistent with deductions from reactive inhibition, except for Number 5, indicating that amount of habituation is inversely related to stimulus strength. At first glance this may seem contradictory, in the sense that response strength is often related to stimulus strength. However, I_r has been developed within the framework of performance variables, where the stimulus events cannot easily be specified, and no close relation between stimulus strength and response amplitude holds. In habituation, particularly of spinal reflexes, initial response strength is directly related to stimulus strength. The increased activation of the response by a stronger stimulus could overcome the I_r buildup. Sherrington's analysis of reflex fatigue (see below) elaborates this point.

Glanzer (1953) showed that deductions from I_r in T-maze alternation behavior appeared to lead to the empirically contracted prediction that subjects will alternate turns even if the discriminable stimuli on the two sides are switched each trial. This has been considered a telling argument against I_r (Dember, 1961; Glanzer, 1953). It seems to us that it may be a rather artificial contradiction resulting from the definition of response which was chosen. From the actual response sequence of running down the alley,

orienting toward and approaching one of the stimulus complexes, and hence turning, Glanzer abstracts turning as the response. If we instead emphasize stimulus *orientation and approach* as the more relevant aspect of the response sequence, then application of Hull's I_r analysis leads to exactly the same predictions as does Glanzer's satiation hypothesis. This characterization of the response, incidentally, is comparable to that used by Spence (1960, p. 374) in his analysis of spatial discrimination learning.

To summarize, I_r is not inconsistent with the phenomena of habituation, and may even be viewed as a molar analysis of the role of response habituation in behavior. Experimentally contradicted predictions made from I_r about alternation behavior may be ascribed to the particular response definition used. The hypothetical neuronal model of habituation developed below might well be considered as a possible neurophysiological basis for certain aspects of I_r .

Fatigue

There is no agreed upon definition of fatigue, either in psychology or physiology. We have defined *effector fatigue* as response decrement localized to neuroeffector and effector processes (cf. Merton, 1954) and shown that it cannot account for habituation, at least of the flexion reflex. It is extremely unlikely that effector fatigue has any great importance for habituation generally since all responses that show habituation can be elicited more strongly, more rapidly, and without decrement under other conditions. As far as central fatigue is concerned, arbitrary definitions specifying certain synaptic states could also be used, but have not come into general parlance. Sherrington's (1906, p. 220) molar definition of reflex fatigue is perhaps the most commonly used: ". . . a spinal

reflex under continuous excitation or frequent repetition becomes weaker, and may cease altogether." He was very careful to hold firmly to this purely operational definition, which is of course identical to the definition of habituation given above. In like manner, Hull (1943, p. 278) identifies reactive inhibition with fatigue, the latter being defined as ". . . decrement in action evocation potentiality *rather than an exhaustion of the energy . . . [italics ours].*"

The inverse relationship between stimulus strength and rate and degree of fatigue or habituation was analyzed very carefully by Sherrington (1906, p. 220):

In my experience, these spinal reflexes fade out sooner under a weak stimulus than under a strong one. This seeming paradox indicated that even under feeble intensities of stimulation the threshold of the reaction gradually rises, and that it rises above the threshold value of the weaker stimulus before it reaches that of the stronger stimulus.

Many students of habituation have argued against fatigue as the mechanism. Most of these have implied effector fatigue (e.g., Harris, 1943; Prosser & Hunter, 1936). However the more general concept of fatigue has also been questioned on the grounds that dishabituation could not occur if a simple fatigue process were responsible for decrement. Such arguments of course make an implicit assumption about the nature of central fatigue; namely, that it is a process which cannot be broken up rapidly by dishabituation. However when dishabituation is viewed as an independent superimposed process (i.e., sensitization), the argument loses its force. Thus in the flexion reflex, response decrement occurs in inter-neuronal pathways without any background change in motor-neuron excitability, but sensitization is commonly

reflected in transient depolarization of motor neurons as well.

In summary, operational definitions of central fatigue do not differ from definitions of habituation and reactive inhibition. Even if this central process is characterized as having a slow recovery time, dishabituation is not a contradiction if viewed as an independent superimposed sensitization process.

THEORETICAL ISSUES—NEURAL

Stimulus Model Comparison

On the basis of a wide variety of ingenious experiments concerning habituation of the human orienting reflex, Sokolov (1960) has developed a theoretical neural schema. While this theory is somewhat specific to the orienting response, it has occasioned widespread interest (cf. Magoun, 1963; Pribam, 1963) and can be generalized to other types of response habituation. In essence it is a feedback comparator analogue. One system (cerebral cortex) is concerned with the formation of a model of the stimulus-input pattern. This interacts with an amplifying system (reticular formation) which serves to alter response tendency. As the model develops in the cortex, reticular amplification is inhibited. If a dishabituating stimulus is given, the amplification is no longer inhibited, and an increased response occurs. The essential point in the theory is that a model of the habituating stimulus activity develops, against which any other stimulus pattern is compared. Response strength is directly proportional to the degree of discordance between any stimulus input and the model.

The crucial experimental observations forming the basis of this theory concern dishabituation by altered stimulus conditions where intensity is not increased. Thus after habituation to a given tone, a weaker tone or a shorter

tone produces dishabituation⁵ of the orienting reflex (Sokolov, 1960). Hence a comparison model is necessary. There are few direct tests of Sokolov's theory. Habituation of the orienting reflex does occur, albeit more slowly, in the totally decorticated animal (Lebidinskaia & Rosenthal, 1935), and auditory orientation habituation occurs in animals without auditory cortex (Thompson & Welker, 1963). These observations tend to raise difficulties for the role of the cortex as the model formation system, but the general construct could still be used by invoking primary sensory relays below the thalamocortical level for the model comparator. In like manner it could be generalized to spinal reflexes by assuming a dual mechanism (as yet unidentified) in cord internuncials.

Perhaps the most important point about the theory is that it may not be necessary to assume a model-comparison process to account for dishabituation by reduced stimulus intensity or altered stimulus characteristic. Coding of intensity in neural networks is complex, and there is not always a simple relation between stimulus intensity and neural activity. Thus in the inferior colliculus and auditory cortex, for any given frequency, some neurons fire to weak tones but not to strong tones (Hind, Rose, Davies, Woolsey, Benjamin, Welker, & Thompson, 1960; Rose, Greenwood, Goldberg, & Hind, 1963). Hence a weak tone will activate cells and synapses not activated by the stronger tone. If habituation is simply some sort of decrease in synaptic efficacy, then a larger response would be expected to a weak tone after habituation to a strong tone because different neurons are activated.

⁵ It should be noted that this is a somewhat special use of the term dishabituation in that the extra stimulus is subsequently used as the test stimulus.

Consequently no sort of comparison against a model is necessary; the process can equally be construed as straightforward decreases in the efficacy of certain pathways, together with differing degrees of pathway overlap resulting from differing stimulus conditions. *Dishabituation by change to a weaker or otherwise altered stimulus then becomes an instance of incomplete stimulus generalization of habituation.* A stimulus having somewhat different central connections than the habituating stimulus yields a larger net response because generalization of habituation to the new stimulus is only partial.

Afferent Neuronal Inhibition

This theory has been elaborated by Hernández-Peón (1955) and has received considerable attention (e.g., Livingston, 1959; Worden & Livingston, 1961). In essence it is assumed that centrifugal fibers from the reticular formation and related structures coursing to various peripheral sensory receptors or nuclei act to inhibit responsiveness at the periphery, thus reducing activity in sensory systems. This inhibition is said to develop during repetitive stimulation and results in evoked response habituation.

There are sound neurophysiological reasons for believing that some types of efferent control systems do exist, although they do not always involve the reticular formation. Two such systems have been described for the auditory system, one acting on the cochlea (Galambos, 1965; Rasmussen, 1946) and one on the cochlear nucleus (Desmedt, 1960; Desmedt & Michelse, 1958). However neither is coextensive with the reticular formation. For the optic system, Granit (1955) has demonstrated both excitatory and inhibitory effects on retinal ganglion cells by stimulation of the midbrain tegmentum. In the somatic system, Hagbarth and Kerr (1954) showed that

reticular stimulation could yield both facilitatory and inhibitory effects on the second-order ascending sensory neurons in the spinal cord. Kerr and Hagbarth (1955) found diminution of olfactory-bulb activity when stimulating a variety of nonreticular structures such as prepyriform cortex, amygdaloid nucleus, and olfactory tubercle.

In sum, efferent control systems appear to exist for all sensory modalities studied. Control is sometimes exerted on early central relays rather than on peripheral receptors and does not always involve the reticular formation. These systems could well provide the basis for habituation of sensory evoked primary responses. Unfortunately, as yet there seems to be no entirely satisfactory or consistent evidence for the occurrence of such habituation (except for rhythmic activity of the olfactory bulb, Moulton, 1963). The further possibility that EEG arousal habituation is so mediated is negated by studies showing comparable habituation phenomena for EEG arousal induced by central electrical reticular stimulation (Glickman & Feldman, 1961) where peripheral gating could not have any role, and by Sharpless and Jasper's (1956) finding that primary evoked responses did not habituate during habituation of EEG arousal to auditory stimuli.

Alterations in Synaptic Transmission

In the course of this article it has been suggested at several points that common neuronal mechanisms may account for many varieties of response habituation. Sherrington (1898, 1906), Prosser and Hunter (1936), Sharpless and Jasper (1956), and Kennedy and Mellon (1964), among others, have all raised the possibility that some type of decrease in synaptic transmission may form the basis of habituation. An hypothetical mechanism will be developed here for the spinal flexion reflex, and its possible

applicability to other systems considered.

It was proved above that habituation of the flexion reflex in the neurally isolated spinal cord must occur in the transmission through interneurons between incoming afferent fibers and output motor neurons. At least three general classes of neural events may be postulated to yield decreased neuron response tendency: synaptic inhibition, decreased synaptic efficacy, or membrane desensitization.

Synaptic Inhibition. Within the category of synaptic inhibition, two general types have been described, postsynaptic inhibition (PostSI), reflected in hyperpolarizing inhibitory postsynaptic membrane potentials, and presynaptic inhibition (PreSI), which acts by depolarizing presynaptic terminals to yield a smaller excitatory postsynaptic potential (Eccles, 1964). These inhibitory mechanisms have been developed for several types of neurons in the spinal cord and are now being established for certain neurons in other portions of the CNS (Eccles, 1964).

Both types of inhibition could be postulated to act on interneurons mediating the flexion reflex. However, the measured time courses of both these types of inhibition (Eccles, 1964) are much too short to summate with 1/second stimulation and to account for effects lasting several minutes. It could be postulated that complex networks involving tonic or cascading and cumulative PreSI or PostSI are activated by the repeated-stimulus pattern. Time relations are still a problem since Gerard and Forbes (1928) were able to detect some homonymous depression up to .8 second after only a single shock (to mixed nerves in their experiment), and we have found a similar depression with a 1-second interval. The time course of known types of Pre- and PostSI is less than about 500 milliseconds. Evidence from pharmacological studies is also against an in-

hibitory hypothesis. Strychnine has been shown to attenuate greatly all types of spinal-cord PostSI on which it has been tested (Eccles, 1964). Picrotoxin has been shown to partially block PreSI (Eccles, 1964). We have found that habituation of the flexion reflex is not significantly altered following administration of these two agents in doses sufficient to obtain the reductions in inhibition just noted. Finally, it may be mentioned that electrical indexes of phasic PreSI (such as the cord-dorsum P wave) and phasic PostSI (hyperpolarizing phases of intracellularly and electrotonically recorded motor-neuron responses) themselves show decrement upon repeated activation of cutaneous afferents (Spencer et al., 1964). The N_1 component of the cord-dorsom response, which itself is highly susceptible to presynaptic inhibition, often shows no decrement during the development of habituation, thus providing further evidence against PreSI. To summarize, all existing evidence points away from inhibition as the agent underlying this type of habituation.⁶

Decreased Synaptic Efficacy. In considering alternative explanations, it is helpful to recall that there are at least two other well-known consequences of reflex action which are quite different from inhibition. The first is a species of synaptic depression variously termed "low frequency depression," "defacilitation," "homosynaptic depression," or "subs synaptic depression" which has been studied in the monosynaptic reflex pathway (Curtis & Eccles, 1960; Jefferson & Schlapp, 1953; Lloyd & Wilson, 1957) and also in some of the simplest disynaptic systems (Wilson,

⁶ However it is to be noted that our experiments were carried out with single-shock stimuli at 1-3-second intervals and that inhibition, particularly the presynaptic variety, may play an important role when higher frequencies are used, as they were in Sherrington's (1899, 1906) studies on fatigue or when intermittent stimulus trains are employed.

1958). Several features of this depression are noteworthy within the context of our discussion: (a) It is manifested as a decrease of PSP amplitude due to intermittent low-frequency synaptic activation and is either pre- or subsynaptic rather than postsynaptic in origin; (b) its time course is too long to be accounted for by presynaptic inhibition (Eccles, Kostyuk, & Schmidt, 1962); and (c) it is detectable at those stimulus intervals required to produce the polysynaptic decrement we have described using single-shock stimuli. The degree of low-frequency depression is greater with increased stimulus frequency, as is the case with habituation. Although Jefferson and Schlapp (1953), recording ventral-root volleys, did report diminished depression with strong stimuli, which would further parallel habituation, Curtis and Eccles (1960), recording motor-neuron excitatory postsynaptic potentials, did not find this effect even with stimuli supramaximal for Group Ia fibers. The depression produced in monosynaptic pathways by low-frequency depression is briefer in duration (less than 20 seconds) than that which we have described. However, it must be remembered that the time course of the depression might be modified in our experiments due to the fact that interneurons characteristically fire in brief trains of discharges, even to single presynaptic volleys, and that this would constitute a distinctly different test pattern which might have a more prolonged recovery period.

The second relevant consequence of reflex action, "after discharge" (Forbes, 1922; Ranson & Hinsey, 1930), is opposite in effect and characteristic of polysynaptic systems. This is manifested as a postsynaptic depolarization and prolonged discharge of inter and motor neurons (Fuortes, 1954; Hunt & Kuno, 1959), is generally more prolonged with stronger stimuli, and may build up with repeated

stimuli (Frank & Fuortes, 1956). Preliminary evidence we have obtained from extracellular interneuron recordings indicates that such afterdischarges are present and build up with stimulus repetition during the processes described.

We would therefore suggest, as a working hypothesis, that the amplitude of repeated polysynaptic test responses depends upon the balance between low-frequency depression and afterdischarge existing at the time each stimulus is presented. Viewed in this way, the frequency sensitivity of the decrement we have described would be related to the well-known frequency sensitivity of low-frequency depression. Stimulus generalization would depend upon depression of interneuron synapses shared by the two input channels. The greater response stability seen at the strong stimulus strengths might reflect a greater preponderance of afterdischarge onto interneurons relaying the reflex. This would increase in duration with strong stimuli and would exist during the presentation of successive stimuli, thereby facilitating the postsynaptic interneuron responses to them, in a sense compensating for the low-frequency depression. Moreover, if the phenomenon of sensitization (i.e., response restoration following a strong extrastimulus) be considered a special case of very prolonged afterdischarge due to a strong stimulus, then many of the puzzling features of this phenomenon could be more readily understood. Wilson's (1955) postulated mechanism of polysynaptic posttetanic potentiation (PTP) is an alternative possibility for sensitization, as is the recently described phenomenon of "presynaptic facilitation" (Kandel & Tauc, 1964; Mendell & Wall, 1965), since there are certain obvious similarities to the process of response restoration we have described.

Membrane Desensitization. We noted earlier that some forms of re-

response habituation, even of spinal reflexes, may last for days or weeks. In the experiment by Kozak et al. (1962), for example, a crossed scratch reflex of the chronic spinal kitten, elicited by rubbing an area of skin for 10 minutes daily, exhibited marked habituation, requiring a period of 8 days to recover. The synaptic processes discussed above, namely inhibition and decreased efficacy due to the balance of low-frequency depression and afterdischarge, would both seem to have too short a time course, per se, to account for such long-lasting habituation. Sharpless (1964) has suggested that a type of membrane desensitization process, involving decreased responsiveness of the postsynaptic membranes of nerve cells due to repeated applications of the transmitter substances, may be involved in long-term habituation. In hypersensitized denervated smooth muscles and glands, for example, administration of appropriate excitatory agents such as epinephrine several times daily produces a desensitization effect that may last for several days (Emmelin & Muren, 1952; Simeone, 1938). This type of hypothesis may be particularly appropriate to the chronic spinal preparation in that spinal reflexes become markedly exaggerated or hypersensitized, as do responses of denervated smooth muscles and glands. Two different classes or components of responses have been distinguished on the basis of habituation and spontaneous-recovery time courses. Sokolov (1955) noted that the "orienting reflex" exhibited both rapidly habituating and slowly habituating components. Sharpless and Jasper (1956) differentiated between a "phasic" EEG arousal that occurs immediately after a stimulus, is of short duration, and is relatively resistant to habituation and a "tonic" component that habituates much more rapidly. Lesions of the brachia of the inferior colliculus appeared to abolish the phasic component (to auditory

stimuli) without eliminating the tonic component. Thompson and Welker (1963) found that ablation of auditory cortex prevented the development of long-term intersession habituation of orienting reflexes to sounds, but did not alter short-term intrasession habituation.

It may well be necessary to postulate at least two different types of neuronal processes to account for short-term and long-term habituation. Our suggested mechanisms of low-frequency depression and afterdischarge are perhaps appropriate to short-term effects and Sharpless' "membrane desensitization" to long-term effects. Alternatively, all these processes may interact to a greater or lesser extent in all instances of habituation. The fact that, except for time course, both short-term and long-term habituation exhibit the same parametric features may imply some identity of underlying processes.

CONCLUSION

In summary, we would suggest that, at least for the spinal flexion reflex as we have studied it, the process of habituation may represent the cumulative effect of a *polysynaptic low-frequency depression* and that dishabituation is a type of *superimposed sensitization*, possibly resulting from facilitatory afterdischarge.

In amplifying this scheme, one might postulate, on the basis of other evidence (Frank & Fuortes, 1956), that rather long iterative trains of interneuron discharges are produced by each stimulus, and that the long duration of the changes noted depends on this feature of the test response. If one provisionally adopts this point of view, several aspects of the literature on habituation reviewed here may be seen in somewhat different perspective. The absence or poor development of evoked response habituation in primary sensory systems would be consistent with the fact that the interneurons exhibiting very

prolonged discharge patterns to single stimuli are not typical of the long relays from receptors to cortex in these systems. However such iterative firing is more characteristic of neurons in the system mediating EEG arousal; the reticular formation (Moruzzi, 1954), which does exhibit habituation (Bell, Sierra, Buendia, & Segundo, 1964; Sharpless & Jasper, 1956). In like manner, such interneurons are undoubtedly present in all functional systems of the intact organism participating in behavioral response habituation.

Other things equal, complex responses tend to habituate more rapidly than simpler responses. If degree of response complexity is reflected in increased numbers of interneurons interposed between stimulus and response, and in an increase in the duration of their repetitive discharges, these factors themselves might account for more rapid habituation. The effects of CNS lesions on behavioral response habituation may also be reconsidered in this way: Effective lesions remove many interneurons normally involved in complex responses and hence could lead to slower response habituation.

Many of these extrapolations from data obtained in the study of response decrement in the spinal cord to habituation as it appears in the more intact organism are obviously speculative. They do have the virtue, however, of indicating the directions which cellular theories of habituation could take. Quantitative theoretical models would clearly be of great help in making such cellular explanations useful alternatives to the more molar theories commonly applied to behavior of the intact organism.

REFERENCES

- ADRIAN, E. D. The electrical activity of the mammalian olfactory bulb. *Electroencephalography and Clinical Neurophysiology*, 1950, 2, 377-388.
- AFELT, Z. Variability of reflexes in chronic spinal frogs. In E. Gutmann & P. Hnik (Eds.), *Proceedings of the conference on central and peripheral mechanisms of motor functions*. Prague, Czechoslovakia: Czechoslovak Academy of Sciences, 1963. Pp. 37-41.
- AFFANNI, J., MANCIA, M., & MARCHIAFAVA, P. L. Role of the pupil in changes in evoked responses along the visual pathways. *Archives Italiennes de biologie*, 1962, 100, 287-296.
- ALTMAN, I. A. Electrophysiological examination of different parts of the auditory system in the cat during sustained rhythmical stimulation. *Sechenov Physiological Journal of the USSR*, 1960, 46, 617-629.
- APELBAUM, J., SILVA, E. E., FRICK, O., & SEGUNDO, J. P. Specificity and biasing of arousal reaction habituation. *Electroencephalography and Clinical Neurophysiology*, 1960, 12, 829-839.
- BARD, P., & MACHT, M. B. The behavior of chronically decerebrate cats. In G. E. W. Wolstenholme & C. M. O'Connor (Eds.), *Neurological basis of behavior*. London: Churchill, 1958. Pp. 55-71.
- BARTLEY, S. H., & CHUTE, E. *Fatigue and impairment in man*. New York: McGraw-Hill, 1947.
- BELL, C., SIERRA, G., BUENDIA, N., & SEGUNDO, J. P. Sensory properties of neurons in the mesencephalic reticular formation. *Journal of Neurophysiology*, 1964, 27, 961-987.
- BERLYNE, D. E. Novelty and curiosity as determinants of exploratory behavior. *British Journal of Psychology*, 1950, 41, 68-80.
- BERLYNE, D. E. *Conflict, arousal, and curiosity*. New York: McGraw-Hill, 1960.
- BINDRA, D. Stimulus change, reactions to novelty, and response decrement. *Psychological Review*, 1959, 66, 96-103.
- BROGDEN, W. J. Animal studies of learning. In S. S. Stevens (Ed.), *Handbook of experimental psychology*. New York: Wiley, 1951. Pp. 568-612.
- BROWN, J. S. *The motivation of behavior*. New York: McGraw-Hill, 1961.
- BUCHWALD, J. S., HALAS, E. S., & SCHRAMM, S. Progressive changes in unit responses to a repeated stimulus. *Federation Proceedings*, 1964, 23, 919.
- BUCHWALD, J. S., HALAS, E. S., & SCHRAMM, S. Progressive changes in efferent unit responses to repeated cutaneous stimulation in spinal cats. *Journal of Neurophysiology*, 1965, 28, 200-215.
- BUTLER, R. A., & HARLOW, H. F. Persistence of visual exploration in monkeys. *Journal of Comparative and Physiological Psychology*, 1954, 47, 258-263.

- CASPERS, H., LERCHE, E., & GREUTER, H. Adaption-serscheinungen der akustisch ausgelösten Weckreaktion bei Reizung mit definierten Tonimpulsen. *Pflüger's Archives*, 1958, **267**, 128-141.
- CAVAGGIONI, A., GIANNELLI, G., & SANTI-BAÑEZ, H. G. Effects of repetitive photic stimulation on responses evoked in the lateral geniculate body and the visual cortex. *Archives Italiennes de biologie*, 1959, **97**, 226-275.
- COOMBS, C. H. Adaptation of the galvanic response to auditory stimuli. *Journal of Experimental Psychology*, 1938, **22**, 244-268.
- CRAMPTON, G. H., & SCHWAM, W. J. Effects of arousal reaction on nystagmus habituation in the cat. *American Journal of Physiology*, 1961, **200**, 29-33.
- CURTIS, D. R., & ECCLES, J. C. Synaptic action during and after repetitive stimulation. *Journal of Physiology*, 1960, **150**, 374-398.
- DAVIS, R. C. Modification of the galvanic reflex by daily repetition of a stimulus. *Journal of Experimental Psychology*, 1934, **17**, 504-535.
- DAVIS, R. C., BUCHWALD, A. M., & FRANKMANN, R. W. Autonomic and muscular responses, and their relation to simple stimuli. *Psychological Monographs*, 1955, **69** (20, Whole No. 405).
- DEMBER, W. N. Response by the rat to environmental change. *Journal of Comparative and Physiological Psychology*, 1956, **49**, 93-95.
- DEMBER, W. N. Alternation behavior. In D. W. Fiske & S. R. Maddi (Eds.), *Functions of varied experience*. Homewood, Ill.: Dorsey, 1961. Pp. 227-252.
- DEMBER, W. N., & EARL, R. W. Analysis of exploratory, manipulatory, and curiosity behavior. *Psychological Review*, 1957, **64**, 91-96.
- DESMEDT, J. E. Neurophysiological mechanisms controlling acoustic input. In G. L. Rasmussen & W. Windle (Eds.), *Neural mechanisms of the auditory and vestibular systems*. Springfield, Ill.: Charles C Thomas, 1960. Pp. 152-164.
- DESMEDT, J. E., & MICHELSE, K. Suppression of acoustic input by thalamic stimulation. *Proceedings of the Society for Experimental Biology and Medicine*, 1958, **99**, 772-775.
- DEUTSCH, J. A. Higher nervous function: The physiological bases of memory. *Annual Review of Physiology*, 1962, **24**, 259-286.
- DYKMAN, R. A., REESE, W. G., GALBRECHT, C. R., & THOMASSON, P. J. Psychophysiological reactions to novel stimuli: Measurement, adaptation, and relationship of psychological variables in the normal human. *Annals of the New York Academy of Sciences*, 1959, **79**, 43-107.
- ECCLES, J. C. *The physiology of synapses*. New York: Academic Press, 1964.
- ECCLES, J. C., KOSTYUK, P. G., & SCHMIDT, R. F. Presynaptic inhibition of the central actions of flexor reflex afferents. *Journal of Physiology* 1962, **161**, 258-281.
- EMMELIN, N., & MUREN, A. The sensitivity of submaxillary glands to chemical agents studied in cats under various conditions over long periods. *Acta Physiologica Scandinavica*, 1952, **26**, 221-231.
- ENGEN, T., & LIPSITT, L. P. Decrement and recovery of responses to olfactory stimuli in the human neonate. *Journal of Comparative and Physiological Psychology*, 1965, **59**, 312-316.
- FERNANDEZ-GUARDIOLA, A., ROLDÁN, E., FANJUL, L., & CASTELLS, C. Role of the pupillary mechanism in the process of habituation of the visual pathways. *Electroencephalography and Clinical Neurophysiology*, 1961, **13**, 564-576.
- FORBES, A. The interpretation of spinal reflexes in terms of present knowledge of nerve conduction. *Physiological Review*, 1922, **2**, 361-414.
- FRANK, K., & FUORTES, M. G. F. Unitary activity of spinal interneurons of cats. *Journal of Physiology*, 1956, **131**, 424-436.
- FRENCH, G. M. Locomotor effects of regional ablations of frontal cortex in rhesus monkeys. *Journal of Comparative and Physiological Psychology*, 1959, **52**, 18-24.
- FRENCH, G. M., & HARLOW, H. F. Locomotor reaction decrement in normal and brain-damaged monkeys. *Journal of Comparative and Physiological Psychology*, 1955, **48**, 496-501.
- FUORTES, M. G. F. Activity of single motor-neurons during some reflex reactions of mammals. *Comptes-Rendus 5th International Neurological Congress* (Lisbon), 1954, **4**, 36-51.
- GALAMBOS, R. Suppression of auditory nerve activity by stimulation of efferent fibers to cochlea. *Journal of Neurophysiology*, 1956, **19**, 424-437.
- GALAMBOS, R., SHEATZ, G., & VERNIER, V. G. Electrophysiological correlates of a conditioned response in cats. *Science*, 1956, **123**, 331-332.
- GARCIA-AUSTT, E. Influence of the states of awareness upon sensory evoked potentials. *Electroencephalography and Clinical Neurophysiology Suppl.* **24**, 1963, 76-89.
- GERARD, R. W., & FORBES, A. "Fatigue" of the flexion reflex. *American Journal of Physiology*, 1928, **86**, 186-205.

- GERSHUNI, G. V., KOZHEVNIKOV, V. A., MARUSEVA, A. M., AVAKYAN, R. V., RADIONOVA, E. Z., ALTMAN, J. A., & SOROKO, V. I. Modifications in electrical responses of the auditory system in different states of the higher nervous system. *Electroencephalography and Clinical Neurophysiology Suppl. 13*, 1960, 115-124.
- GLANZER, M. Stimulus satiation: An explanation of spontaneous alternation and related phenomena. *Psychological Review*, 1953, 60, 257-268.
- GLASER, E. M., & GRIFFIN, J. P. Influence of the cerebral cortex on habituation. *Journal of Physiology*, 1962, 160, 429-445.
- GLICKMAN, S. E. Deficits in avoidance learning produced by stimulation of the ascending reticular formation. *Canadian Journal of Psychology*, 1958, 12, 97-102.
- GLICKMAN, S. E., & FELDMAN, S. M. Habituation of the arousal response to direct stimulation of the brainstem. *Electroencephalography and Clinical Neurophysiology*, 1961, 13, 703-709.
- GRANIT, R. Centrifugal and antidromic effects on ganglion cells of retina. *Journal of Neurophysiology*, 1955, 18, 388-411.
- GREEN, J. D., & ARDUINI, A. A. Hippocampal electrical activity in arousal. *Journal of Neurophysiology*, 1954, 17, 533-557.
- GRIFFIN, J. P. The role of the frontal areas of the cortex upon habituation in man. *Clinical Science*, 1963, 24, 127-134.
- GRIFFITH, C. R. The effect upon the white rat of continued bodily rotation. *American Naturalist*, 1920, 54, 524-534.
- GUZMÁN-FLORES, C., ALCARAZ, M., & HARMONY, T. Role of the intrinsic ear muscles in the process of acoustic habituation. *Boletín del Instituto de estudios médicos y biológicos, Universidad nacional de México*, 1960, 18, 135-149.
- HAGAMEN, W. G., LANCE, E. M., & UNGEWITTER, L. H. Increased responsiveness to stimuli following lesions of the forebrain. *Anatomical Record*, 1959, 133, 387-388.
- HAGBARTH, K. E., & FINER, B. L. The plasticity of human withdrawal reflexes to noxious skin stimuli in lower limbs. In G. Moruzzi, A. Fessard, & H. H. Jasper (Eds.), *Progress in brain research*. Vol. 1. *Brain mechanisms*. New York: Elsevier, 1963. Pp. 65-81.
- HAGBARTH, K. E., & KERR, D. I. B. Central influences on spinal afferent conduction. *Journal of Neurophysiology*, 1954, 17, 295-307.
- HAGBARTH, K. E., & KUGELBERG, E. Plasticity of the human abdominal skin reflex. *Brain*, 1958, 81, 305-318.
- HARRIS, J. D. Habitatory response decrement in the intact organism. *Psychological Bulletin*, 1943, 40, 385-422.
- HERNÁNDEZ-PEÓN, R. Central mechanisms controlling conduction along central sensory pathways. *Acta neurologica latinoamericana*, 1955, 1, 256-264.
- HERNÁNDEZ-PEÓN, R. Neurophysiological correlates of habituation and other manifestations of plastic inhibition. *Electroencephalography and Clinical Neurophysiology Suppl. 13*, 1960, 101-114.
- HERNÁNDEZ-PEÓN, R., GUZMÁN-FLORES, C., ALCARAZ, M., & FERNÁNDEZ-GUARDIOLA, A. Habituation in the visual pathway. *Acta neurologica latinoamericana*, 1958, 4, 121-129.
- HERNÁNDEZ-PEÓN, R., JOUVET, M., & SCHERRER, H. Auditory potentials at cochlear nucleus during acoustic habituation. *Acta neurologica latinoamericana*, 1957, 3, 144-156.
- HERNÁNDEZ-PEÓN, R., LAVIN, A., ALCOCERCUARÓN, C., & MARCELIN, J. P. Electrical activity of the olfactory bulb during wakefulness and sleep. *Electroencephalography and Clinical Neurophysiology*, 1960, 12, 41-58.
- HERNÁNDEZ-PEÓN, R., & SCHERRER, H. Habituation to acoustic stimuli in cochlear nucleus. *Federation Proceedings*, 1955, 14, 71.
- HERNÁNDEZ-PEÓN, R., SCHERRER, H., & VELASCO, M. Central influences on afferent conduction in the somatic and visual pathways. *Acta neurologica latinoamericana*, 1956, 2, 8-22.
- HILGARD, E. R., & MARQUIS, D. G. *Conditioning and learning*. New York: Appleton-Century-Crofts, 1940.
- HIND, J. E., ROSE, J. E., DAVIES, P. W., WOOLSEY, C. N., BENJAMIN, R. M., WELKER, W. I., & THOMPSON, R. F. Unit activity in the auditory cortex. In G. L. Rasmussen & W. Windle (Eds.), *Neural mechanisms of the auditory and vestibular systems*. Springfield, Ill.: Charles C Thomas, 1960. Pp. 201-210.
- HINDE, R. A. Changes in responsiveness to a constant stimulus. *British Journal of Animal Behavior*, 1954, 2, 41-55.
- HUGELIN, A., DUMONT, S., & PAILLAS, N. Tympanic muscles and control of auditory input during arousal. *Science*, 1960, 131, 1371-1372.
- HULL, C. L. *Principles of behavior*. New York: Appleton-Century-Crofts, 1943.
- HUMPHREY, G. Extinction and negative adaptation. *Psychological Review*, 1930, 37, 361-363.
- HUMPHREY, G. *The nature of learning*. New York: Harcourt, Brace, 1933.

- HUNT, C. C., & KUNO, M. Properties of spinal interneurons. *Journal of Physiology*, 1959, **147**, 346-363.
- HUTTENLOCHER, P. R. Effects of state of arousal on click responses in the mesencephalic reticular formation. *Electroencephalography and Clinical Neurophysiology*, 1960, **12**, 819-827.
- JAMES, W. *Principles of psychology*. New York: Holt, 1890.
- JEFFERSON, A., & SCHLAPP, W. Some effects of repetitive stimulation of afferents on reflex conduction. In J. L. Malcolm & J. A. B. Gray (Eds.), *The spinal cord*. London: Churchill, 1953. Pp. 99-119.
- JOUVET, M., & HERNÁNDEZ-PEÓN, R. Mécanismes neurophysiologiques concernant l'habituation, l'attention, et le conditionnement. *Electroencephalography and Clinical Neurophysiology Suppl.* **6**, 1957, 39-49.
- KANDEL, E. R., & TAUC, L. Mechanisms of prolonged heterosynaptic facilitation. *Nature*, 1964, **202**, 145.
- KENNEDY, D., & MELLON, D., JR. Synaptic activation and receptive fields in crayfish interneurons. *Comparative Biochemistry and Physiology*, 1964, **13**, 275-300.
- KERR, D. I. B., & HAGBARTH, K. E. An investigation of olfactory centrifugal fiber system. *Journal of Neurophysiology*, 1955, **18**, 362-374.
- KIMBLE, G. A. *Hilgard and Marquis' conditioning and learning*. New York: Appleton-Century-Crofts, 1961.
- KNOTT, J. R., & HENRY, C. E. The conditioning of the blocking of the alpha rhythm of the human electroencephalogram. *Journal of Experimental Psychology*, 1941, **28**, 134-144.
- KONORSKI, J. *Conditioned reflexes and neuron organization*. New York: Cambridge Univ. Press., 1948.
- KOZAK, W., MACFARLANE, W. W., & WESTERMAN, R. Longlasting reversible changes in the reflex responses of chronic spinal cats to touch, heat and cold. *Nature*, 1962, **193**, 171-173.
- KRECHEVSKY, I. Brain mechanisms and variability: I. Variability within a means-end-readiness. *Journal of Comparative Psychology*, 1937, **23**, 121-138. (a)
- KRECHEVSKY, I. Brain mechanisms and variability: II. Variability where no learning is involved. *Journal of Comparative Psychology*, 1937, **23**, 139-163. (b)
- KRECHEVSKY, I. Brain mechanisms and variability: III. Limitations of the effect of cortical injury upon variability. *Journal of Comparative Psychology*, 1937, **23**, 351-364. (c)
- LEBEDINSKAIA, S. I., & ROSENTHAL, J. S. Reactions of a log after removal of the cerebral hemispheres. *Brain*, 1935, **58**, 412-419.
- LEHNER, G. F. J. A study of the extinction of unconditioned reflexes. *Journal of Experimental Psychology*, 1941, **29**, 435-456.
- LETHLEAN, A. K. Habituation in the rat spinal cord—a triggered process. *Federation Proceedings*, 1965, **24**, 517.
- LIVINGSTON, R. B. Central control of receptors and sensory transmission. In J. Field (Ed.), *Handbook of physiology: Section 1. Neurophysiology*. Vol. 1. Washington, D. C.: American Physiological Society, 1959. Pp. 741-760.
- LLOYD, D. P. C., & WILSON, V. J. Reflex depression in rhythmically active monosynaptic reflex pathways. *Journal of General Physiology*, 1957, **40**, 409-426.
- LOMBARD, W. P. The variations of the normal knee jerk and their relation to the activity of the central nervous system. *American Journal of Physiology*, 1887, **1**, 5-71.
- MAGOUN, H. W. Central neural inhibition. In M. R. Jones (Ed.), *Nebraska symposium on motivation: 1963*. Lincoln: Univ. Nebraska Press, 1963. Pp. 161-196.
- MANCIA, M., MEULDERS, M., & SANTI-BAÑEZ-H., G. Changes of photically evoked potentials in the visual pathway of the cerveau isolé cat. *Archives Italiennes de biologie*, 1959, **97**, 378-398.
- MARSH, J. T., MCCARTHY, D. A., SHEATZ, G., & GALAMBOS, R. Amplitude changes in evoked auditory potentials during habituation and conditioning. *Electroencephalography and Clinical Neurophysiology*, 1961, **13**, 224-234.
- MARSH, J. T., & WORDEN, F. G. Auditory potentials during acoustic habituation: Cochlear nucleus, cerebellum and auditory cortex. *Electroencephalography and Clinical Neurophysiology*, 1964, **17**, 685-692.
- MARSH, J. T., WORDEN, F. G., & HICKS, L. Some effects of room acoustics on evoked auditory potentials. *Science*, 1962, **137**, 281-282.
- MARTIN, I. Adaptation. *Psychological Bulletin*, 1964, **61**, 35-44.
- MELZACK, R. On the survival of Mallard ducks after "habituation" to the hawk-shaped figure. *Behavior*, 1961, **17**, 1-16.
- MENDELL, L. M., & WALL, P. D. Presynaptic hyperpolarization: A role for fine afferent fibers. *Journal of Physiology*, 1965, **172**, 274-294.
- MERTON, P. A. Voluntary strength and fatigue. *Journal of Physiology*, 1954, **123**, 553-564.
- MONTGOMERY, K. C. Exploratory behavior as a function of "similarity" of stimulus situations. *Journal of Comparative and*

- Physiological Psychology*, 1953, **46**, 129-133.
- MORGAN, C. T., & WOOD, W. M. Cortical localization of symbolic processes in the rat: II. Effect of cortical lesions upon delayed alternation in the rat. *Journal of Neurophysiology*, 1943, **6**, 173-180.
- MORRELL, F. Electrophysiological contributions to the neural basis of learning. *Physiological Review*, 1961, **41**, 443-494.
- MORUZZI, G. The ascending reticular activating system and wakefulness. In J. F. Delafresnaye (Ed.), *Brain mechanisms and consciousness*. Oxford: Blackwell, 1954. Pp. 1-20.
- MOULTON, D. G. Electrical activity in the olfactory system of rabbits with indwelling electrodes. In Y. Zotterman (Ed.), *Olfaction and taste*. New York: MacMillan, 1963. Pp. 71-84.
- MOUSHEGAN, G., RUPERT, A., MARSH, J., & GALAMBOS, R. Evoked cortical potentials in absence of middle ear muscles. *Science*, 1961, **133**, 582.
- MOWRER, O. H. The modification of vestibular nystagmus by means of repeated elicitation. *Comparative Psychology Monographs*, 1934, **9**(45).
- NAQUET, R., REGIS, H., FISCHER-WILLIAMS, M., & FERNANDEZ-GUARDIOLA, A. Variations in the responses evoked by light along the specific pathways. *Brain*, 1960, **83**, 52-56.
- NESMEIANOVA, T. N. The inhibition of the motor reflex in spinal dogs under conditions of chronic experimentation. *Sechenov Journal of Physiology of the USSR*, 1957, **42**, 281-288.
- PALESTINI, M., DAVIDOVICH, A., & HERNÁNDEZ-PEÓN, R. Functional significance of centrifugal influences upon the retina. *Acta neurologica latinoamericana*, 1959, **5**, 113-131.
- PAVLOV, I. P. *Conditioned reflexes*. (Trans. by G. V. Anrep) London: Oxford, 1927.
- PORTER, J. M. Adaptation of the galvanic skin response. *Journal of Experimental Psychology*, 1938, **23**, 553-557.
- PRIBRAM, K. H. Reinforcement revisited: A structural view. In M. R. Jones (Ed.), *Nebraska symposium on motivation: 1963*. Lincoln: Univer. Nebraska Press, 1963. Pp. 113-160.
- PROSSER, C. L., & HUNTER, W. S. The extinction of startle responses and spinal reflexes in the white rat. *American Journal of Physiology*, 1936, **117**, 609-618.
- RANSON, S. W., & HINSEY, J. C. Reflexes in the hind limbs of cats after transection of the spinal cord at various levels. *American Journal of Physiology*, 1930, **94**, 471-495.
- RASMUSSEN, G. L. The olivary peduncle and other fiber projections of the superior olivary complex. *Journal of Comparative Neurology*, 1946, **84**, 141-219.
- RHINEBERGER, M., & JASPER, H. H. Electrical activity of the cerebral cortex in the unanesthetized cat. *American Journal of Physiology*, 1937, **119**, 186-196.
- ROBERTS, W. W., DEMBER, W. N., & BRODWICK, M. Alternation and exploration in rats with hippocampal lesions. *Journal of Comparative and Physiological Psychology*, 1962, **55**, 695-700.
- ROBINSON, E. S. Work of the integrated organism. In C. Murchison (Ed.), *A handbook of general experimental psychology*. Worcester, Mass.: Clark Univer. Press, 1934. Pp. 571-650.
- ROBINSON, J., & GANTT, W. H. The orienting reflex (questioning reaction): Cardiac, respiratory, salivary, and motor components. *Bulletin of the Johns Hopkins Hospital*, 1947, **80**, 231-253.
- RODGERS, W. L., MELZACK, R., & SEGAL, J. R. "Tail flip response" in goldfish. *Journal of Comparative and Physiological Psychology*, 1963, **56**, 917-923.
- ROIG, J. A., & SOMMER-SMITH, J. A. Atenuación específica del sobresalto provocado par excitación nerviosa central. *Anales de la Facultad de medicina, Universidad de Montevideo*, 1959, **44**, 410-413.
- ROSE, J. E., GREENWOOD, D. D., GOLDBERG, J. M., & HIND, J. E. Some discharge characteristics of single neurons in the inferior colliculus of the cat: I. Tonotopical organization, relation of spike-counts to tone intensity, and firing patterns of single elements. *Journal of Neurophysiology*, 1963, **26**, 294-320.
- SANTIBAÑEZ, G., TROUCHE, E., & ALBE-FESSARD, D. Étude de l'évolution au cours du temps de l'amplitude des activités corticales et thalamiques évoquées par des stimuli somatique répétés. *Journal de Physiologie*, 1963, **55**, 335.
- SCHOLANDER, T. Habituation of autonomic response elements under two conditions of alertness. *Acta physiologica scandinavica*, 1960, **50**, 259-268.
- SCHWARTZBAUM, J. S., WILSON, W. A., JR., & MORRISSETTE, J. R. The effects of amygdalotomy on locomotor activity in monkeys. *Journal of Comparative and Physiological Psychology*, 1961, **54**, 334-336.
- SEGUNDO, J. P., ROIG, J. A., & SOMMER-SMITH, J. A. Conditioning of reticular

- formation stimulation effects. *Electroencephalography and Clinical Neurophysiology*, 1959, **11**, 471-484.
- SHARPLESS, S. K. Reorganization of function in the nervous system—use and disuse. *Annual Review of Physiology*, 1964, **26**, 357-388.
- SHARPLESS, S., & JASPER, H. Habituation of the arousal reaction. *Brain*, 1956, **79**, 655-682.
- SHAW, J. A., & THOMPSON, R. F. Dependence of evoked cortical association responses on behavioral variables. *Psychonomic Science*, 1964, **1**, 153-154.
- SHERRINGTON, C. S. Experiments in examination of the peripheral distribution of the fibers of the posterior roots of some spinal nerves. *Royal Society of London*, 1898, **190**, 45-186.
- SHERRINGTON, C. S. *The integrative action of the nervous system*. New Haven: Yale Univ. Press, 1906.
- SHURRAGER, P. S., & CULLER, E. Conditioned extinction of a reflex in the spinal dog. *Journal of Experimental Psychology*, 1941, **28**, 287-303.
- SHURRAGER, P. S., & SHURRAGER, H. C. Converting a spinal CR into a reflex. *Journal of Experimental Psychology*, 1941, **29**, 217-224.
- SIMEONE, F. A. Responsiveness of denervated nictitating membrane. *American Journal of Physiology*, 1938, **122**, 650-658.
- SOKOLOV, E. N. The higher nervous activity and the problem of perception. *Proceedings of the XIX International Congress of Psychology*, Montreal, 1955.
- SOKOLOV, E. N. Neuronal models and the orienting influence. In M. A. B. Brazier (Ed.), *The central nervous system and behavior: III*. New York: Macy Foundation, 1960.
- SOLOMON, R. L. The influence of work on behavior. *Psychological Bulletin*, 1948, **45**, 1-40.
- SPENCE, K. W. *Behavior theory and learning*. Englewood Cliffs, N. J.: Prentice-Hall, 1960.
- SPENCER, W. A., THOMPSON, R. F., & NEILSON, D. R. Analysis of polysynaptic reflex response decrement in the acute spinal cat. *Physiologist*, 1964, **7**, 262.
- SYMMES, D. Anxiety reduction and novelty as goals of visual exploration by monkeys. *Journal of Genetic Psychology*, 1959, **94**, 181-198.
- SYMMES, D. Effect of cortical ablations on visual exploration by monkeys. *Journal of Comparative and Physiological Psychology*, 1963, **56**, 757-763.
- THOMPSON, R. F., & SHAW, J. A. Behavioral correlates of evoked activity recorded from association areas of the cerebral cortex. *Journal of Comparative and Physiological Psychology*, 1965, **60**, 329-339.
- THOMPSON, R. F., & WELKER, W. I. Role of auditory cortex in reflex head orientation by cats to auditory stimuli. *Journal of Comparative and Physiological Psychology*, 1963, **56**, 996-1002.
- THORPE, W. H. *Learning and instinct in animals*. London: Methuen, 1956.
- VORONIN, L. G., & SOKOLOV, E. N. Cortical mechanisms of the orienting reflex and its relation to the conditioned reflex. *Electroencephalography and Clinical Neurophysiology Suppl.* **13**, 1960, 335-346.
- WALKER, E. L. Action decrement and its relation to learning. *Psychological Review*. 1958, **65**, 129-142.
- WEBSTER, W. R., DUNLOP, C. W., SIMONS, L. A., & AITKIN, L. M. Auditory habituation: A test of a centrifugal and a peripheral theory. *Science*, 1965, **148**, 654-656.
- WELKER, W. I. Variability of play and exploratory behavior in chimpanzees. *Journal of Comparative and Physiological Psychology*, 1956, **49**, 181-185.
- WELKER, W. I. An analysis of exploratory and play behavior in animals. In D. W. Fiske & S. R. Maddi (Eds.), *Functions of varied experience*. Homewood, Ill.: Dorsey, 1961. Pp. 175-226.
- WENDT, G. R. Vestibular functions. In S. S. Stevens (Ed.), *Handbook of experimental psychology*. New York: Wiley, 1951. Pp. 1191-1223.
- WILSON, V. J. Post-tetanic potentiation of polysynaptic reflexes of the spinal cord. *Journal of Genetic Physiology*, 1955, **39**, 197-206.
- WILSON, V. J. Early post-tetanic potentiation and low frequency depression of some group I reflex actions. *Journal of Genetic Physiology*, 1958, **41**, 1005-1018.
- WORDEN, F. G., & LIVINGSTON, R. B. Brainstem reticular formation. In D. E. Sheer (Ed.), *Electrical stimulation of the brain*. Austin: Univ. Texas Press, 1961. Pp. 263-276.
- WORDEN, F. G., & MARSH, J. T. Amplitude changes of auditory potentials evoked at cochlear nucleus during acoustic habituation. *Electroencephalography and Clinical Neurophysiology*, 1963, **15**, 866-881.

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