reactions. This explanation would be consistent with radioautographic data of delayed hypersensitivity of the skin (*9*) and with the findings that MIF-rich supernatants, when injected into the skin, produce an infiltrate of mononuclear cells (*6*). It is also possible that the mononuclear cells, having reached the site to which they have been attracted, are prevented from leaving that site by the action of MIF. The possibility that supernatants from antigen-stimulated lymphocytes are chemotactic for other types of leukocytes and the relation of the chemotactic factor to MIF and to other known factors that are chemotactic for mononuclear cells remain unanswered questions.

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Stimulus Properties of Reinforcing Brain Shock

Abstract. *Rats easily discriminate between two types of subcortical brain shock which differ in reinforcing properties. When both stimuli are either neutral or positively reinforcing subjects have difficulty in responding differentially to the two types of electrical stimulation of the brain. Possible implications for a theory concerning a generalized or diffuse reinforcement system are discussed.*

The perceptual properties of intracranial reinforcement are an almost completely neglected aspect of the phenomenon of self-stimulation. Rewarding septal and hypothalamic brain shock does not differ markedly (if at all) from auditory signals when used as conditioned stimuli in experiments on avoidance learning in a shuttle box (*1*); thus it is reasonable to assume that rewarding the electrical stimulation to the brain (ESB) has stimulus or cue properties. As a next logical step, it seems important to compare the stimulus characteristics of the reinforcement produced by electrical stimulation of various brain sites.

In self-stimulation experiments we may be tapping the neural substrate of conventional biological drive and reward (*2*). For example, several brain sites producing rewarding effects when stimulated also elicit "stimulus-bound" eating, drinking, or copulation (*3*). Furthermore, self-stimulation rates in certain areas appear to be modulated by specific drive and hormonal conditions (*4*). Self-stimulation at various anatomical points may involve the activation of several *different* reward systems. Therefore, one might assume that animals readily discriminate among different types of rewarding ESB just as they discriminate among conventional rewards.

In our experiment we attempted to establish rewarding brain shock in one locus as a discriminative stimulus (S^D) for response emission in a task motivated by hunger and rewarded by food. Reinforcing ESB in another locus served as S^A, indicating to the animal that the food reward was not available.

Twelve male albino rats were implanted with two bipolar stimulating electrodes and were tested for self-stimulation at both sites. In all subjects, one electrode was aimed at the diagonal band of Broca, and the other was placed in either the medial forebrain bundle-lateral hypothalamus or in the ventral tegmental nucleus (Tsai), as described elsewhere (*5*). In three subjects, both electrodes produced positively reinforcing effects (+,+); in three other rats both electrodes were "neutral" (0,0); and in the remaining six, one of the electrodes was reinforcing while a second electrode was "neutral" (+,0). In the self-stimulation tests and in all subsequent phases of the experiment, both electrodes were stimulated at the same intensity.

After the self-stimulation tests, subjects were placed on a 23-hour schedule of food deprivation and were trained to press a lever to obtain food pellets (45 mg). Once this response was learned the rats were gradually placed on a reinforcement schedule of 11 responses for one reinforcement (FR 11 : 1), and several daily 10-minute sessions were given until response rates stabilized. Six additional 10-minute sessions were then given during which subjects continued to respond for food on the FR 11 : 1 schedule, except that noncontingent, pulsing brain shock was delivered through alternate electrodes throughout the session. The electrical stimulation to the brain was 60 hz, pulsed 0.3 seconds on, 3.0 seconds off, at the intensity determined for each subject during the earlier self-stimulation tests. The stimulation was delivered in 1-minute trains through one electrode at a time, according to a predetermined random order. Thus, on each of 6 days, the rats received five 1-minute trains of brain stimulation through each electrode while working for food on the FR 11 : 1 schedule. This phase of training was included because previous studies had indicated that noncontingent ESB frequently interferes with ongoing behavior. During this phase stable base rates of responding were established for assessing later behavior.

During the final phase of the experiment, discrimination training, subjects

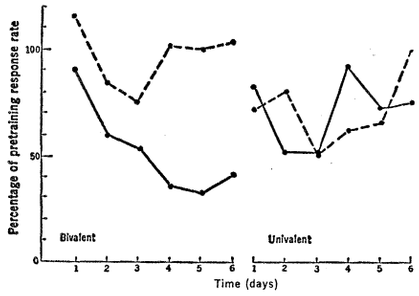

Fig. 1. Percentage of pretraining response rate to S^D (dashed line) and S^Δ (solid line) during 6 days of discrimination training; 100 percent represents response rate before discrimination training.

continued to work for food during the presentation of ESB as in the previous phase, except that responses occurring during stimulation at one locus were no longer reinforced. Thus, we attempted to establish one locus of brain shock as a discriminative stimulus (S^D) while the second locus of brain stimulation signaled that food was temporarily unavailable (S^Δ). Which stimulus locus served as S^D and which as S^Δ was randomly determined for each subject. This phase of the experiment was continued for 6 days after which subjects were killed.

Microscopic examination confirmed that in all subjects one of the electrodes was located in the diagonal band of Broca. In six rats the second electrode was located either directly in the medial forebrain bundle (MFB) or the immediately adjacent lateral hypothalamic area bordering on MFB. Five other subjects had the second electrode in the ventral tegmental nucleus, and two rats had electrodes in the hippocampus. The various combinations of electrodes were fairly evenly distributed over the four groups (*6*).

The relative discriminability of the stimuli was assessed by comparing the difference in response rates during the presence of S^D and S^Δ for the various groups over the 6 days of training. In the statistical analyses, the difference scores were adjusted to take into consideration any prediscrimination differences in lever pressing during the two types of stimulation. Therefore, response rates are expressed as percentages of the original base-level responding. Four groups were available for the analysis. In group ++ both stimuli (S^D and S^Δ) were rewarding; in group 00 both stimuli were neutral; in group 0+ S^D was neutral and S^Δ was rewarding; in group +0 S^D was rewarding but S^Δ was neutral.

A groups times days analysis of variance showed a significant groups main effect ($F = 4.31$; d.f. $= 3,9$; $P < .05$) although the days main effect and the groups times days interaction were not significant. Postmortem tests (Scheffé) indicated that groups ++ and 00 did not differ from each other, nor did groups 0+ and +0. Groups ++ and 00 combined differed significantly, however, from groups 0+ and +0 combined, so for graphic presentation these subgroups were reclassified as univalent (++,00) and bivalent (+0, 0+). When S^D and S^Δ differed in their reinforcing properties, the discrimination occurred almost immediately (Fig. 1). For the univalent group, on the other hand, the discrimination did not begin to occur until the final session.

Our results, that ESB in two rewarding (or in two neutral) loci are not readily discriminable while two subcortical stimuli differing in reward value were discriminated almost immediately, are generally consistent with a previous experiment (with different technique for studying other loci) wherein it was concluded that a very salient aspect of the cue properties of limbic system stimulation is the presence or absence of reward effects (*7*). From a theoretical orientation, one might ask if the centrally elicited reward phenomenon is the result of a diffuse or generalized satisfying state of affairs, or whether the type of reward differs as a function of the anatomical structure being stimulated.

Our findings disclose the possibility that many of the diverse structures which support self-stimulation are part of a generalized or undifferentiated reward system. The fact that massive lesions of the central nervous system fail to attenuate self-stimulation behavior (*8*) also suggests that some type of mass-action equipotentiality principle may be operative within the self-stimulation system.

Earlier studies (*3*) which pointed to the possible functional identity of structures producing self-stimulation and specific consummatory behavior also might be reconsidered in the light of recent results. For example, identical stimulation in areas implicated in the self-stimulation phenomenon may elicit either eating, drinking, or gnawing behavior depending on learning factors and the momentary environmental conditions (*9*), thus suggesting that in some cases even centrally produced stimulus-bound motivated behavior may be the result of a nonspecific readiness to respond. Similarly, it has been shown that although stimulation through a single electrode may elicit both self-stimulation and drinking, these two types of behavior were affected differentially (and in some cases in opposite directions) by lesions and drugs (*10*). Finally, the published verbal reports of humans receiving apparently rewarding ESB contain no references to specific types of pleasure but only to a diffuse feeling of relaxation or great satisfaction (*11*).

Our results and the possible theoretical implications are preliminary, although we obtained consistent findings when comparing septal-hippocampal (*7*), septal-medial forebrain bundle, septal-lateral hypothalamic, and septal-tegmental self-stimulation sites.

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