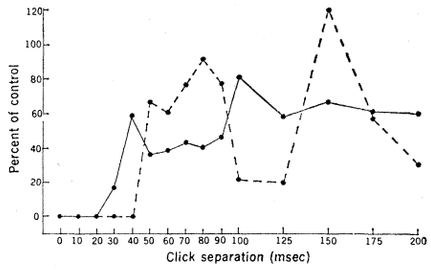

Fig. 2. Recovery amplitude curve for second of two paired clicks compared with control amplitude of single clicks. Broken line, with barbiturate (Nembutal); solid line, without barbiturate (awake). Each point is based on the peak amplitude of the average of 50 responses.

then injected with barbiturate (*10*), and a control was recorded which consisted of 50 responses averaged to stimuli given at the rate of 1 per 10 seconds. Each animal was then stimulated for 30 minutes at the rate of 1 per second, and 50 responses were averaged every 5 minutes.

The results showed a significant difference ($t = 8.37$, $P < .01$) between the unanesthetized (Fig. 1D) and the injected controls (Fig. 1E). This difference in amplitude and waveform was similar to that produced in the first experiment. This indicates that changes due to barbiturates can be obtained without intervening repetitive stimulation at rates known to produce habituation. There were also significant amplitude decrements (shown by the test of trend) during a 30-minute stimulation at 1 per second in animals given barbiturate (Fig. 1F).

All animals showed amplitude and waveform changes caused by barbiturates, but three animals showed marked waveform changes exhibiting cyclic spindling or reverberatory activity. This waveform consisted of gradually declining rhythmic activity with a period of approximately 100 msec. To determine the nature of this cyclic activity, the three animals were tested in a paired-click experiment (*12*), in which functions of recovery amplitude for the second of two paired clicks were determined both with and without barbiturate. To achieve this, 50 paired responses were averaged on the computer for each of a range of intervals between the two clicks. There are marked differences between recovery curves for anesthetized and unanesthetized animals (Fig. 2). The recovery curve obtained for the injected animal shows an initial depression in recovery followed by a facilitation, then another depression in recovery followed by a facilitation. The evoked potential to the second of a pair of clicks can be facilitated or depressed according to where in the phase of the activity induced by the first click the response to the second click arrives. The cyclic activity consists of alternate peaks of excitation and inhibition. Similar findings have been reported in the ventrobasal complex and the medial geniculate (*13*).

Recovery in the medial geniculate of unanesthetized animals is relatively slow (Fig. 2). Complete recovery from the effects of the first click often takes several seconds, a finding similar to that reported for the auditory cortex (*14*). Taken in conjunction with the evidence for a rate effect with repetitive stimulation (*1–3*) these data are in keeping with the proposition that auditory habituation is based on long-term synaptic inhibition. In fact, so called habituation decrements in the auditory pathway might be better interpreted as being due to a refractory process based on inhibition intrinsic to the particular auditory area.

In the medial geniculate this inhibition may be based on recurrent postsynaptic inhibition because a similar mechanism has been put forward to explain both barbiturate spindling in the ventrobasal complex (*15*) and depression of recovery in the lateral geniculate (*16*). It could also be argued that all these effects are due to tonic inhibitory activity arising in the reticular formation (*17*), and that barbiturates merely block this inhibition. This interpretation is unlikely because there is evidence (*13, 18*) that barbiturate spindling occurs in the isolated thalamus when all connections with the reticular formation have been severed, and amplitude decrements occur under barbiturates (Fig. 1F).

Changes in medial geniculate evoked potentials produced by barbiturates cannot be interpreted as abolishing habituation (*4*) or preventing habituation (*5*), because similar changes occur without repetitive stimulation. Furthermore, habituation of medial geniculate evoked potentials might be produced by inhibition intrinsic to this area (possibly recurrent postsynaptic inhibition). This interpretation would indicate that the decrements are more akin to a refractory phenomenon than to a true habituation process (*19*).

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References and Notes

1. W. R. Webster, C. W. Dunlop, L. A. Simons, L. M. Aitkin, *Science* **148**, 654 (1965).
2. L. A. Simons, C. W. Dunlop, W. R. Webster, L. M. Aitkin, *Electroencaphalogr. Clin. Neurophysiol.* **20**, 485 (1966).
3. J. D. Cook, E. H. Ellinwood, Jr., W. P. Wilson, *Exp. Neurol.* **21**, 167 (1968).
4. R. Hernández-Peón, M. Jouvet, H. Scherrer, *Acta Neurol. Lat. Amer.* **3**, 144 (1957).
5. I. A. Al'tman, *Sechenov Physiol. J. USSR* (English Transl.) **46**, 617 (1960).
6. R. S. Snider and W. T. Niemer, *A Stereotaxic Atlas of the Cat Brain* (Univ. of Chicago Press, Chicago, 1961).
7. W. R. Webster and C. W. Dunlop, *J. Audit. Res.* **5**, 11 (1965).
8. Mnemotron computer of average transients, model 400B.
9. Twenty millisecond burst of pulses (1000 per second) of 105-db peak sound pressure level with reference to .0002 microbar, measured by a General Radio impact noise analyzer (type 1556-A) and a General Radio sound level meter (type 1551-B).
10. Intraperitoneal injection of Nembutal (45 mg/kg).
11. B. J. Winer, *Statistical Principles in Experimental Design* (McGraw-Hill, New York, 1962), pp. 365–369.
12. One-tenth millisecond clicks of 100-db peak sound pressure level with reference to .0002 microbar.
13. P. Andersen, S. A. Andersson, T. Lomo, *J. Physiol.* **192**, 257 (1967); ———, *ibid.* p. 283.
14. M. R. Rosenzweig and W. A. Rosenblith, *Psychol. Monogr.* **67**, 1 (1953).
15. P. Andersen, J. C. Eccles, T. A. Sears, *J. Physiol.* **174**, 370 (1964).
16. A. J. Sefton and W. Burke, *Nature* **205**, 1325 (1965).
17. L. M. Aitkin, C. W. Dunlop, W. R. Webster, *J. Neurophysiol.* **19**, 109 (1966).
18. F. Bremer, *C. R. Seances Soc. Biol.* **118**, 1235 (1935).
19. R. F. Thompson and W. A. Spencer, *Psychol. Rev.* **173**, 16 (1966).
20. Supported by grants from the National Health and Medical Council of Australia and the Australian Research Grants Committee.

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Intracranial Self-Stimulation and the Rapid Decline of Frustrative Nonreward

Abstract. *Animals deprived of reward for a task previously rewarded behave differently, depending on whether the reward is food or positive brain stimulation. Unlike the relatively stable frustration effects obtained with conventional reward, frustration produced by withholding brain stimulation dissipates rapidly with time.*

Behavior reinforced with conventional rewards has been compared with that obtained by intracranial self-stimulation (ICS) (*1*). When behavior is controlled by central stimulation it has often been reported (*2*) that performance is impaired on simple learning tasks involving schedules of reinforcement and rates of extinction. However, some investigators (*3*) have found that some of the differences seem to disappear when procedural details are more closely controlled in order to make the comparisons more

meaningful. Other differences, such as sharp performance decrements with ICS after short time intervals (*4*), are not typical of conventional learning and remain to be explained.

Our experiment is designed to test the generality of time-based performance decrements with ICS with the use of the conventional frustration paradigm (*5*) not yet tested with brain stimulation. Amsel and Roussel trained rats to traverse two runways in succession with food reward in goal boxes at the end of each section. After a history of reinforcement in both goal boxes, the animals were then deprived of reward in the first goal box on selected test trials. After this "frustration," subjects ran significantly faster in the second runway. This energizing of behavior that follows nonreward was termed the frustration effect (FE), and it was further hypothesized that the magnitude of the FE would be a function of confinement time without reward in goal box No. 1. A test of this hypothesis, however, led them to conclude that confinement times of 5 to 30 seconds produced consistent and stable FE's. If rewarding brain stimulation is the "same" as conventional reward, it would be expected that similar FE's would be obtained with ICS. If the rewarding effects of ICS dissipate rapidly with time, the FE's should decrease as confinement time increases.

Six male albino rats (Charles River strain) were implanted with bipolar electrodes (0.356 mm in diameter) aimed at the lateral hypothalamus. After the experiment, staining of brain sections with cresyl violet confirmed the placements. The apparatus was a modified double runway 2.44 m in length with a goal box enclosed at the middle and at the end. A fixed lever in each goal box could be pushed five times on each trial with every response resulting in 0.3 second of sine wave stimulation of about 185 μa. Running time to goal box No. 2 was measured over 0.76 m in the second runway by timers triggered by photoelectric cells. In pretraining, rats learned to press a lever for ICS in an apparatus outside the runways, and a current level was established which would maximize the reinforcement value. The procedures of Amsel and Roussel were followed as closely as possible in training animals to run to each goal box for ICS.

Subjects were used as their own controls in order to minimize possible differences due to electrode sites. Each rat was tested in six sessions, one for each combination of motivational state (20 to 23 hours hungry and fed) and confinement period (5, 15, and 25 seconds). All combinations of conditions were balanced across days and rats to control for possible sequencing effects. In each session, stable running speed in runway 2 was first obtained after about 50 trials in which ICS was delivered for bar pressing in both goal boxes. The criterion was five successive trials in which running time did not vary more than $\pm$ 0.03 second. Then 18 experimental trials were run including nine control trials and nine randomly presented test trials (frustration trials) in which ICS was not delivered after lever pressing in goal box No. 1. Running times to goal box No. 2 for the nine test trials and nine control trials were compared for each of the six conditions. The intertrial interval was 45 seconds, and each rat was given five noncontingent pulses of ICS in the start box at the beginning of each trial to control for possible aftereffects of the previous trial (ten reinforcements on control trials and only five on test trials).

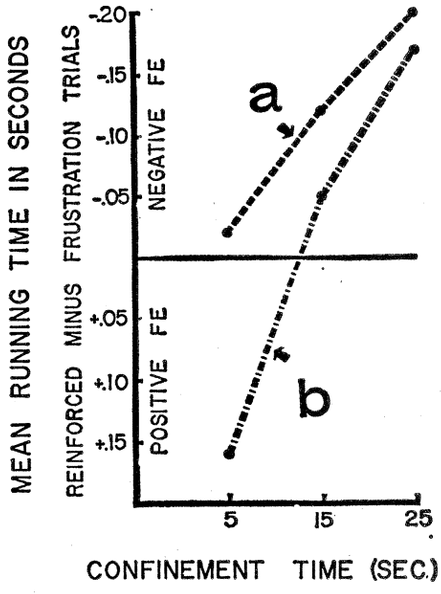

Fig. 1. Mean running time to goal box No. 2 as a function of confinement time in goal box No. 1. A positive frustration effect (FE) indicates that subjects ran faster to goal box No. 2 after nonreinforcement in goal box No. 1 than after reinforcement. (a) fed freely; (b) hungry.

The magnitude of the FE is a function of confinement time in goal box No. 1 (Fig. 1). With the running time during the nine unrewarded control trials for each animal used as a reference (0.0 FE), it can be seen that when subjects were hungry and confined for 5 seconds they ran faster to the second goal box. This positive FE is significant ($t = 3.45$, d.f. 5, $P < .05$, correlated t-test), but is eliminated when the same animals are tested after 15 seconds confinement. At 25 seconds, there is a suggestion of a reverse or negative effect ($P < .10$). When the rats were fed and tested after a 5- or 15-second confinement, there was no significant FE. At 25 seconds, however, a significant negative FE ($P < .05$) was obtained, indicating that the animals ran more slowly after frustration trials.

These findings are different from those obtained with conventional reinforcement. Amsel and Roussel (*5*) suggested that with food reward the FE is greatest when the confinement time is 10 seconds, but continues to be significant for 30 seconds. Later MacKinnon and Amsel (*6*) reported a maximum FE at about 15 seconds, with dissipation apparent after 90 seconds. In contrast to the relatively stable drive produced by frustrative nonreward, our results show that, if the reinforcer is ICS, frustration dissipates completely in 15 seconds and becomes a reverse effect after 25 seconds. The possibility that ICS might have aversive components can be ruled out by an experiment (*7*) in which animals with similar electrode placements failed to make any avoidances of 0.5-second pulses of ICS after intertrial intervals of 5, 15, 30, or 60 seconds.

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References and Notes

1. J. Olds, *J. Comp. Physiol. Psychol.* **49**, 507 (1956); J. Kling and Y. Matsumiya, *Science* **130**, 668 (1962); J. Panksepp and J. Trowill, *Psychon. Sci.* **9**, 407 (1967); J. Kling and M. Berkeley, *J. Comp. Physiol. Psychol.* **65**, 507 (1968); R. Johnson, in preparation.
2. See C. Gallistel, *Psychol. Bull.* **61**, 23 (1964).
3. W. Gibson, L. Reid, M. Sakai, P. Porter, *Science* **148**, 1357 (1965); S. Pliskoff, J. Wright, T. Hawkins, *J. Exp. Anal. Behav.* **8**, 75 (1965); J. Huston, *Science* **159**, 444 (1968).
4. C. Gallistel, *Psychon. Sci.* **9**, 167 (1967); R. Johnson, *J. Comp. Physiol. Psychol.* **66**, 422 (1968); J. Panksepp, R. Gandelman, J. Trowill, *Psychon. Sci.* **13**, 135 (1968).
5. A. Amsel and J. Roussel, *J. Exp. Psychol.* **43**, 363 (1952).
6. J. MacKinnon and A. Amsel, *ibid.* **67**, 468 (1964).
7. R. Johnson and R. Levy, *Psychon. Sci.* **14**, 106 (1969).
8. Supported by NIH grant MH 16147-01.

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