Cortical spreading depression and habituation¹

LYNN NADEL
McGILL UNIVERSITY

Habituation of exploratory activity in a novel situation was studied in rats under several conditions of cortical spreading depression. The results suggest the tentative conclusion that the cortex is not necessary for temporary storage of information pertaining to the stimulus situation, but is needed for permanent storage of this same information.

Early attempts to condition an avoidance response in animals with bilateral cortical spreading depression (BSD) indicated that the cortex was necessary for such training (Bureš, Burešová, & Záharová, 1958; Travis & Sparks, 1963). However, more recent studies have shown that avoidance learning can occur without functional cortex (Thompson, 1964; Thompson & Hjelle, 1965), suggesting "subcortical learning." To test the generality of "subcortical learning" the present study sought to determine whether habituation of exploratory responses could occur under conditions of spreading depression.

Method

Subjects. Thirty-five male hooded rats, weighing between 220 and 300 gm at the time of operation, were used in this study. Ss were housed individually and maintained on an ad libitum food and water schedule throughout the study.

Operative procedure. Two cannulae were surgically implanted in the skull of each rat, one being located over each parietal cortex, approximately 3 mm posterior to bregma and 2 mm lateral to the midline. The cannula assembly consisted of a flanged polyethylene tube within a hollow stainless steel set screw, with a steel cap-nut covering the screw to prevent evaporation of the contents. The bottoms of the flanged tubes rested on the dural membrane. These cannulae were used for the administration of KCl to one or both hemispheres, bringing about unilateral or bilateral spreading depression. Between testing sessions the cannulae were kept filled with NaCl.

Apparatus. Testing for habituation consisted of placing each S for 15 min. in a box (8 x 12 x 8 in.), with wooden walls, Plexiglas lengths, a Plexiglas top and a grid floor. The Plexiglas lengths were covered with black and white stripes. Activity within the box was measured by the Peacock-Williams ultrasonic activity device, which consists of two transducers, mounted atop the box, one emitting an ultrasonic signal, the other picking it up. This apparatus measures distortions in the signal caused by movements within the box, rectifies and amplifies these distortions and emits pulses which are registered on counters. In the present study, activity counts were registered separately for each minute of the 15-min. daily test session. These counts were summed over 5-min. blocks, yielding three scores for each S for the daily 15-min. test session.

Testing procedure. Daily tests of exploratory activity began two days after the surgical operation and lasted for six days. Ss were divided into five groups, as follows: (1) Group BSD-BSD was tested on all six sessions under bilateral spreading depression (N=5); (2) Group BSD-NSD was tested on the first three under BSD and on the last three after saline injection, the NSD condition (N=9); (3) Group NSD-BSD was tested on the first three under NSD and on the last three under BSD (N=9); (4) Group NSD-NSD was tested on all six after saline injection (N=6); and, (5) Group USD-USD was tested on all six under unilateral spreading depression, the same hemisphere being depressed on all six days (N=6).

Animals that were to be subjected to spreading depression on a given test day had KCl injected into their cannulae 15 min. before

Fig. 1. Mean activity score per minute for the three main treatment groups (BSD-BSD, NSD-NSD and USD-USD) for the six test sessions.

testing began; those under NSD were given NaCl injections. Animals injected with KCl were checked for the effectiveness of spreading depression by noting the impairment of placing reactions in the limbs contralateral to the hemisphere being depressed. Ss not demonstrating such a loss were discarded; four rats in all were discarded for this reason.

Results and Discussion

Figure 1 displays the mean activity score per minute for the three main treatment groups (NSD-NSD, BSD-BSD and USD-USD) over the six test sessions. BSD Ss showed an increase in activity, while the NSD Ss showed a decrease. USD Ss did not show a reliable decrease ($p > .10$) but did show a tendency in this direction. An analysis of variance indicated that there was a significant interaction between treatments and sessions ($F = 3.99$, $df = 10/70$, $p < .01$). Clearly, there was no intersession habituation in the case of the BSD-BSD group.

Table 1 provides intrasession habituation ratios for the three groups, the ratios being computed from the formula $R = B/(B + A)$, where A is the activity score for the initial 5-min. block of the daily test session and B is the activity score for the final 5-min. block of the session. This ratio can vary between 0 and 1, with 0.5 being equal to no change, values below 0.5 indicating

Table 1. Mean daily intrasession habituation ratios

Group	Test Sessions					
	1	2	3	4	5	6
BSD	.174	.189	.167	.276	.228	.291
NSD	.452	.393	.479	.234	.351	.311
USD	.341	.418	.293	.487	.352	.359

habituation, and values above 0.5 indicating an increase in activity. These data demonstrate quite clearly that BSD Ss were as good, if not better than the other treatment groups in terms of intrasession habituation. Thus, though BSD Ss showed no habituation from session to session they were quite capable of habituation within any given session.

Habituation to novel stimulation may be viewed as consisting of two processes: the formation of a neuronal model corresponding to the stimulus situation, and the inhibition of (exploratory) activity upon the presentation of a stimulus that matches that internal model. The fact that BSD animals demonstrated intrasession habituation indicates that the cortex is not crucially involved in the inhibition of activity. The lack of intersession habituation would therefore seem related in some way to the elaboration of the neuronal model.

Motor effects produced by spreading depression provide an alternative interpretation of the deficit in intersession habituation. BSD Ss were, at first, considerably less active than either NSD or USD Ss. This lower initial activity may have masked any habituation that might have taken place in the situation. However, the hypothesis of a deficit in the elaboration of the neuronal model appears more plausible for two reasons. First, Jouvett (1961) has shown that the cortex is essential for habituation of both the EEG arousal reaction and the orienting reaction in cats. Further, he demonstrated that there was a direct relationship between the rate of habituation and the amount of functional cortex left intact. The present data, on habituation of exploration, are thus consistent with previous findings concerning the role of the cortex in habituation. Second, if subcortical storage of the neuronal model were possible it would lead to the following predictions about the two transfer groups, NSD-BSD and BSD-NSD: (1) animals first tested under BSD would show very rapid habituation when switched to NSD, more rapid than that shown in animals first tested under NSD; and, (2) animals first tested under NSD would show a stable rate of activity when switched to BSD. An analysis of variance, latin-square design, was

performed on the data from these groups to determine if the predictions were upheld. The interaction between treatments and sessions (interpretable as a three-way interaction among spreading depression condition, presence or absence of prior testing, and test sessions) was not significant ($F=0.98$, $df=2/32$). This indicates that prior testing under BSD does not yield more rapid habituation in NSD Ss, nor does prior testing under NSD yield more stable levels of activity under BSD. Thus, the predictions generated by the subcortical storage hypothesis are not confirmed.

The present study indicates that animals with bilateral spreading depression are capable of both temporary memory storage and the inhibition of behavioral activity. However, the cortex seems to be crucial for permanent memory storage in the present situation. Generalizations about the nature and site of learning formed on the basis of studies employing only aversive motivation should be made cautiously, at least until evidence has been provided that similar results will obtain in situations involving other motivational systems.

References

- Bureš, J., Burešová, O., & Zaharová, A. Conditioned reflexes and Leao's spreading cortical depression. *J. comp. physiol. Psychol.*, 1958, 51, 263-268.
- Jouvett, M. Recherches sur les mecanismes neurophysiologiques du sommeil et de l'apprentissage negatif. In A. Fessard, R. W. Gerard, and J. Konorski (Eds.), *Brain mechanisms and learning*. Springfield, Ill.: C. C. Thomas, 1961, Pp. 445-479.
- Thompson, R. W. Transfer of avoidance learning between normal and functionally decorticate states. *J. comp. physiol. Psychol.*, 1964, 57, 321-325.
- Thompson, R. W., & Hjelle, L. A. Effects of stimulus and response complexity on learning under bilateral spreading depression. *J. comp. physiol. Psychol.*, 1965, 69, 122-124.
- Travis, R. P., & Sparks, D. L. The influence of unilateral and bilateral spreading depression during learning upon subsequent relearning. *J. comp. physiol. Psychol.*, 1963, 56, 56-59.

Notes

1. This research was supported by a grant (APT-74) from the National Research Council of Canada to Dr. Dalbir Bindra.
2. Completion of the manuscript took place while the writer was a United States Public Health Service Predoctoral Fellow.