Biphasicity of the time-response curve and amnesic effect of electroconvulsive shock in passive avoidance conditioning*

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Mice were trained in a one-trial passive avoidance task and retested 2 min, 5 min, 10 min, 30 min, or 24 h later. A biphasic time-response curve was obtained with an initial increase to 5 min, a subsequent decrease, and another increase to 24 h. Other groups of Ss were administered electroconvulsive shock (ECS) 2, 5, 10, or 30 min after training and retested 24 h later. The response curve shape of the ECS-treated groups was found to correspond to that concerning the different retest times, suggesting a negative correlation between ECS amnesic effect and the strength of the conditioned response at the time of ECS administration. The inadequacy of the hypotheses, according to which ECS interferes with a gradual monotonic process, to explain ECS amnesic effect is discussed.

A well established finding in the studies on the effect of electroconvulsive shock (ECS) administration upon memory processes is the time dependency of this effect. The shorter the time interval between learning experience and ECS administration, the worse the subsequent performance by which the retention of the learning experience is assessed.

Different explanations of this temporal gradient have been proposed, based on the notions of memory trace consolidation (McGaugh, 1966), of aversiveness of ECS (Coons & Miller, 1960), of conditioned inhibition (Lewis & Maher, 1965), of the arousal-eliciting properties of the footshock used in the learning situation (Schneider & Sherman, 1968), and of incubation of the conditioned response (Pinel & Cooper, 1966a, b). While the second and third hypotheses have been proved to be inappropriate in most cases and the fourth is applicable only to very short temporal gradients, the consolidation and the incubation hypotheses appear to be the most valid presently.

The main assumption of the consolidation hypothesis is that, following a learning experience, a memory trace is formed and gradually strengthened with the passage of time. The temporal gradient produced by an amnesic treatment is thus explained by hypothesizing that a more consolidated memory trace is more resistant to the treatment.

The incubation hypothesis, on the contrary, is based on a directly demonstrable phenomenon, that is, the gradual increase of the strength of the conditioned

response over time following learning. The temporal gradient is explained by hypothesizing that a stronger conditioned response is more resistant to the amnesic treatment.

The problem is that both hypotheses predict the same monotonic increasing temporal gradient after ECS administration, i.e., the same gradual impairment in performances with decreasing time intervals between learning and ECS administration. This makes the experimental differentiation between the two hypotheses difficult.

Zerbolio (1969) and Robustelli et al (1970), however, have recently found a biphasic time-response curve for a one-trial passive avoidance response. This response first increases after learning, decreases subsequently, and then increases again.

The existence of biphasic time-response curves cannot be considered in agreement with the incubation notion. Consequently, while the incubation notion has been used so far to provide an explanation for the temporal gradient produced by ECS administration alternative to that offered by the consolidation hypothesis, it is proposed that a more general hypothetical alternative to that of the memory trace consolidation might be one in which ECS effect is dependent on the strength of the conditioned response at the time of ECS administration, whatever the time-response curve is.

The purpose of the present study is to use the biphasic time-response curve to test the validity of this hypothesis vs the consolidation hypothesis in explaining the time-dependent memory deficits produced by ECS administration. According to the consolidation hypothesis, ECS administration at different times after

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Fig. 1. Retest trial latency medians. The solid line represents the latency medians of the groups retested at different times after training. The dashed line represents the latency medians of the groups administered ECS at different times after training and retested 24 h later. In the abscissa are indicated the time intervals between training and retest for the control groups and between training and ECS administration for the treated groups.

learning should result in a monotonic increasing temporal gradient, whatever is the temporal variation of the strength of the conditioned response. On the contrary, the hypothesis according to which ECS effect depends on the strength of the conditioned response at the time of ECS administration predicts no monotonic increasing temporal gradient but rather a nonmonotonic one, with a shape corresponding to the normal time-response curve obtained retesting the Ss at different times after learning.

MATERIALS AND METHOD

Subjects

The Ss were 603 female CFI albino mice, approximately 6 weeks old, housed eight to a cage, with ad lib access to food and water.

Apparatus

Animals were trained in a step-through apparatus consisting of a trough-shaped two-compartment box made of 5.6-mm Plexiglas plates (Jarvik & Kopp, 1967). In the smaller transparent compartment, Ss were exposed to a bright Tensor lamp approximately 2 cm away. The smaller compartment was connected to the larger darkened compartment by an opening 3.2 x 2.7 cm wide and flush with the floor. The opening could

be closed by a guillotine door. The floor of the smaller compartment (8 x 3.2 cm) consisted of a pair of parallel metal plates. The floor of the larger compartment (18 x 3.2 cm) consisted of two pairs of plates bent up to form the side walls. One of the two pairs of plates was 8 cm long, the other pair of plates was 10 cm long. Adjacent plates were 2-3 mm apart. At the top, the two compartments widened to 10 x 10 and 10 x 18 cm, respectively, and were covered with hinged Plexiglas lids. Each pair of parallel plates in the larger compartment was bridged when the animal stood on it.

Procedure

The Ss were placed into the smaller lighted compartment facing away from the door, and they stepped spontaneously into the larger darkened compartment. A timer was started manually when the animal was placed in the apparatus and was stopped automatically when the S crossed a photocell on the wall of the larger compartment, 8 cm from the opening. A 350- μ amp footshock was automatically delivered through both sets of metal plates in the larger compartment at the moment the photocell beam was interrupted and the Ss escaped from the dark compartment back into the lit compartment, from which they were removed. The measure of retention of the passive avoidance behavior is assumed to be the length of time the S remains in the safe compartment in the retest trial, the procedure of which is identical to that followed in the training trial. Animals who remained longer than 600 sec were removed.

Electroconvulsive shock (15 m amp for 0.2 sec) producing full tonic seizures was administered transcorneally, outside the conditioning apparatus, using a Hans electroshock apparatus (2-C).

Nine groups of 67 animals each were used. The five control groups were retested, respectively, 2 min, 5 min, 10 min, 30 min, and 24 h after training. The four treated groups were given ECS, respectively, 2, 5, 10, or 30 min after training and were all retested 24 h after training. Thus, the real control group to assess the amnesic effect of ECS is the group not given ECS and tested 24 h after training, while the other control groups indicate the strength of the conditioned response at the time ECS was administered to the treated groups.

RESULTS

A Kruskal-Wallis analysis of variance showed no significant differences in the training trial latencies among all nine groups. The results of the retest trials are represented in Fig. 1. It appears that they show an initial increase to 5 min, a subsequent decrease, and another increase to 24 h. A similarly shaped time-response curve was obtained considering either the retest times in the four control groups or the times at which ECS was administered in the three treated groups. A Kruskal-Wallis analysis of variance performed upon the five control groups showed a significant effect of time of retest ($p < .001$). The same analysis performed upon the four treated groups showed a significant effect of time of ECS administration ($p < .02$). Multiple comparisons (Wilcoxon & Wilcox, 1964) within both the control and the treated groups showed that the retest latencies of the peak groups (5 min and 24 h for the control; 5 min for the treated) differ significantly from those of their adjacent groups [for the control groups, 2 min vs 5 min and 30 min vs 24 h ($p < .01$), 10 min vs 5 min ($p < .05$); for the treated groups, 2 min vs 5 min ($p < .01$), 10 min

vs 5 min ($p < .05$). Comparisons (Wilcoxon & Wilcox, 1964) between each ECS group and the 24-h control group reveal significantly lower retest latencies for all ECS groups ($p < .01$). The latencies of the retest trial are significantly higher ($p < .01$) than those of the training trial in each group, indicating that the passive avoidance conditioned response was formed and, at least partially, retained in all nine groups.

DISCUSSION

The results of the present experiment show the same biphasic response curve when the Ss are retested at a given time after training as when they are administered ECS at that time and retested 24 h after training, suggesting a negative correlation between ECS effect and the strength of the conditioned response at the time of ECS administration.

This finding indicates the inadequacy of the hypothesis of memory trace consolidation to explain ECS amnesic effect. More generally, any traditional notion implying ECS interference with a gradual monotonic process, either consolidation of memory trace or incubation of conditioned response, cannot account for the results obtained in the present study.

The biphasicity of the time-response curve has been considered by Zerbolio (1969) as indicative of a two-stage memory formation. In this context, the time-dependent amnesic effect of ECS could be thought to be related to the consolidation of both short- and long-term memory traces, being less when either memory trace is more consolidated. Thus, a high degree of memory storage by itself, independent of the specific memory system involved, would be the necessary and sufficient condition for a trace to be resistant to ECS administration.

It would be more reasonable, however, to consider the nonmemory aftereffects of the learning situation the most crucial factors in determining time-response curves (at least for the first 24 or 48 h), probably by affecting response mechanisms. In fact, it is difficult to assume that memory processes can have such different time courses, as reflected by the very different time-response curves that have been obtained (incubation gradients, biphasic curves, Kamin effect), while these curves seem to be more easily accounted for in terms of consequences of the arousing and stressing properties of the various learning situations. In this case, the time-dependent effect of ECS could result from the interaction between ECS administration and particular physiological-biochemical conditions due to the nonmemory aftereffects of the learning experience. Such interaction is likely to affect response mechanisms. A more complex interaction, however, between ECS administration, particular physiological-biochemical conditions consequent to the nonmemory aftereffects of the learning situation, and memory processes can also be hypothesized.

A previous finding by Suboski and Weinstein (1969)

of an ECS-maintained Kamin effect might also be explained on the basis of the general hypothesis of a negative correlation between ECS effect and the strength of the conditioned response at the time of ECS administration. Unfortunately, the basic control group is missing in that study to assess any real amnesic effect of ECS, and the ECS-treated groups were retested at variable time intervals after learning. Thus, no conclusive comparison with the present study is possible. On the other hand, Suboski and Weinstein's mere incubation-disruption notion cannot be applied to the finding of the present study. In fact, a monotonic incubation process can account for the Kamin effect in active avoidance conditioning, according to Denny and Ditchman (1962), while it cannot explain the biphasic time-response curve of passive avoidance conditioning in which two successive incubation-like processes appear.

Finally, the results of the present study suggest that the usual monotonic increasing temporal gradients produced by ECS administration are nothing but a particular case of the ECS time-dependent effect, which is obtained when the time-response curve is a monotonic function or, rather, when the time intervals between learning and ECS that have been chosen would produce a monotonic function if the Ss were retested at the end of these intervals rather than given ECS.

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