Electroconvulsive shock induced amnesia and recovery¹

ANNE GELLER AND M. E. JARVIK

ALBERT EINSTEIN COLLEGE OF MEDICINE, NEW YORK

Recovery from electroconvulsive shock (ECS) induced amnesia in mice did not occur with time alone or with multiple trials in a stepthrough apparatus, although attempts were made to increase the probability of such recovery. Subjects receiving foot shock (FS) and ECS always show significantly higher latencies than unshocked controls and this difference can be increased using a threshold FS after extinction.

There has been considerable controversy in the literature as to whether ECS can induce retrograde amnesia (RA) at all (Lewis & Maher, 1965) and, if it does, whether it is effective given more than 10 sec from the training trial (Chorover, 1965), and recently, whether there is recovery from this apparent amnesia. Zinkin & Miller (1967) found that in a step-down apparatus with rats, recovery from amnesia observed at 24 h occurred if the animals were given additional reinforced trials at 48 and 72 h. Luttges & McGaugh (1967) found this not to be true for mice using a step-through apparatus.

The period of RA in man following concussion frequently shrinks spontaneously during recovery (Russell & Nathan, 1946) although there is usually an irreducible few seconds of amnesia. The recovery observed by Zinkin and Miller in rats following ECS may be analogous. It seemed reasonable that the probability of recovery might be increased if the interval between training and ECS were extended and if the animals were allowed to explore the apparatus extensively prior to training. It also seemed possible that a threshold FS might reveal "latent learning" in apparently amnesic animals.

EXPERIMENT 1

Subjects

The Ss were 138 naive CF1 female mice, 6-8 weeks old, and were housed eight to a cage with ad lib access to food and water.

Apparatus and Procedure

The step-through apparatus was that described by Jarvik & Kopp (1967) and consisted of a trough shaped two compartment box in which the animal could receive a 500 mA FS for stepping from a small lighted compartment to a larger darkened one. The Ss escaped from the FS back to the light compartment from which they were removed. Retest trials were run with the same procedure except no shock was used and the Ss, if they stepped through, were removed from the black compartment.

Through transcorneal electrodes, ECS was administered 20 sec after the training trial. A Hans

electroshock apparatus (2-C) was used with convulsive shock of 20 mA for .2 sec.

Subjects were discarded from the experiment for the following reasons: (1) latency greater than 60 sec on training trial (7 Ss); (2) failure to have full tonic clonic convulsions (2 Ss); (3) death (2 Ss).

The Ss were divided into the following groups: Group C (N=10) received no treatment. They were run in the apparatus on the training day and at 24, 48, 72, and 168 h. All other Ss received FS on the training day. Half the Ss (A groups) received no further treatment; the other half (B groups) received ECS 20 sec after the punishing shock. The Ss were then subdivided according to their testing schedule. Group 1A (N=15) and 1B (N=13) were tested at 24, 48, 72, and 168 h. Group 2A (N=15) and 2B (N=13) were tested at 48, 72, and 168 h. Group 3A (N=14) and 3B (N=13) were tested at 72 and 168 h. Group 4A (N=16) and 4B (N=16) were tested at six weeks.

Results

The usual criterion of retention in a step-through experiment is the length of time S remains in the front compartment. In this experiment all the A groups (FS-no ECS) had a median of >300 sec (arbitrary cutoff) on first retest except 4A (median 200) and all the B groups (FS-ECS) had medians less than 60 on the first retest. At all time intervals, the FS group had a higher median latency than its partner ECS group, and this was significant at the < .005 level (Wilcoxon et al, 1963) for all test pairs at all time intervals. Furthermore, there was a tendency for the median latencies for all groups to decline with successive trials, which might be expected since any animal that steps through and does not get shocked has an extinction trial. Differences for Group 1B between the first trial (24 h) and the fourth trial (168 h) are significant at < .005 level. No significant differences were observed between the first trials of 1B (24 h), 2B (48 h), 3B (72 h), and 4B (6 weeks). Significant differences at the < .005 level were also noted between the FS-ECS groups and the nonshocked controls for all time intervals for which they were tested.

For the nonshocked control groups, steady step-through latencies were obtained for all trials and individual fluctuations in latency did not exceed 16 sec. For the FS-ECS groups, 69% showed fluctuations > 20 sec and of these, 26% showed an increase of > 20 sec of Trial 2, 3, or 4 over Trial 1.

EXPERIMENT 2

This experiment examined the effects of preliminary exposure to the apparatus.

Subjects

The Ss were 50 naive CF1 female mice, 6-8 weeks old.

Apparatus and Procedure

The apparatus was the same as that used in Experiment 1. All animals were given 5 min of exposure to the apparatus daily for four days. They were then divided into the following groups: Group 1 (N=17; control unshocked) were run in the apparatus on Days 5, 6, 7, 8 and removed as soon as they had stepped into the black compartment. Group 2 (N=16) received a 500 mA FS on stepping through on Day 5 and were tested on Days 6, 7, and 8. Group 3 (N=17) were treated as Group 2, but were given transcorneal ECS 20 sec after the shocked trial on Day 5.

Results

Differences between Group 2 (FS) and Group 3 (FS-ECS) were significant at the $< .005$ level for Days 6, 7, and 8. Median latencies of both groups were lower than in Experiment 1. The FS-ECS group again showed a decline in latencies over the three trials. Medians for the NS control and the FS-ECS group were 7.2 and 11.5 sec, respectively, compared with FS median of 20.2 sec. Differences between the control and ECS groups were significant at the $< .025$ level.

EXPERIMENT 3

Subjects

The Ss were 34 animals from Groups 2 and 3 of Experiment 2.

Apparatus and Procedure

The apparatus was the same as that used in Experiments 1 and 2. The Ss were allowed to explore the apparatus without shock 5 min daily for four days after the conclusion of Experiment 2. The median step-through latency for Group 1 was 5.7 and for Group 3 4.1 on Day 4. The difference was not significant. On Day 5 all Ss received a threshold FS (50 mA) on stepping into the black compartment.

Results

Median latency on Day 6 was 27.0 sec for Group 1 and 58.3 sec for Group 3. This was significant at the $< .005$ level.

DISCUSSION

Using mice in a step-through apparatus there does

not seem to be any overall evidence for recovery of the ECS induced amnesia either with time or with multiple trials, even under conditions designed to increase the probability of such recovery. Three possible explanations for the recovery observed by Zinkin & Miller (1967) occur: (1) ECS does not induce a true RA but has some nonspecific "fear reducing" motor activity effects which dissipate with time; (2) ECS does induce true RA and the recovery is analogous to that seen in postconcussion RA; and (3) that ECS induces only a partial amnesia (i.e., some aversive conditioning remains) and this can be reinforced or extinguished over several trials depending upon the experimental technique.

To avoid the latter explanation, recovery must be shown to occur with time alone. If this is found to be the case with rats and not mice, then one might assume that the fear reducing or motor activity effects of ECS are permanent in one species and transitory in another. Or alternatively, there may be shrinkage of RA with time but the time relations vary among species. Perhaps in the mouse, a smaller animal with a higher rate of metabolism, potential recovery is essentially completed at 24 h so that no further recovery can be demonstrated at longer time intervals.

References

- CHOROVER, S. L., & SCHILLER, P. H. Short term retrograde amnesia in rats. *J. comp. physiol. Psychol.*, 1965, 59, 73-78.
- JARVIK, M. E., & KOPP, R. An improved one-trial passive avoidance learning situation. *Psychol. Rpts.*, 1967, 21, 221-224.
- LEWIS, D. J., & MAHER, B. A. Neural consolidation and electroconvulsive shock. *Psychol. Rev.*, 1965, 72, 225-239.
- LUTTGES, M. W., & MCGAUGH, J. L. Permanence of retrograde amnesia produced by ECS. *Science*, 1967, 156, 408-410.
- RUSSELL, W. R., & NATHAN, P. W. Traumatic amnesia. *Brain*, 1946, 69, 280-300.
- WILCOXON, F., KATTI, S. K., & WILCOX, R. A. Critical values and probability levels for the Wilcoxon Rank Sum Test and the Wilcoxon Rank Test. Lederle Laboratories Division, American Cyanamid Co., August, 1963.
- ZINKIN, S., & MILLER, A. J. Recovery of memory after amnesia induced by ECS. *Science*, 1967, 155, 102-104.

Notes

1. Fuller details on this experiment can be obtained from Dr. Geller on request.
2. This work was supported by U. S. Public Health Service Grants MH 01225, MH 05319 and 5T1 MH 6418.