Whether or not a defect or defects exist in the mediation of a "signal(s)" from the insulin-receptor complex to biological effectors of insulin actions as suggested by this investigation remains to be proved. However, this study has shown that insulin resistance in large adipocytes is not a problem arising from defective insulin binding but that, as in other insulin-resistant states (*13*), the defect or defects occurs in processes subsequent to insulin-cell association.

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Retrieval Failure Induced by Electroconvulsive Shock: Reversal with Dissimilar Training and Recovery Agents

Abstract. *Amnesia was obtained following electroconvulsive shock in rats trained at one-trial passive avoidance of immersion in ice water. Avoidance behavior was restored when noncontingent foot shock was administered outside the training apparatus. The qualitative differences between ice water and foot shock demonstrate that the agent inducing recovery of memory need not be physically similar to the reinforcer used during training. These findings are interpreted as supporting a retrieval failure view of experimental amnesia.*

Considerable research has focused on the problem of the permanence of retrograde amnesia induced by electroconvulsive shock (ECS). The traditional view maintains that ECS produces an irreversible loss of memory (*1*). In accordance with this view, most studies looking for spontaneous recovery of memories impaired by ECS have been unsuccessful (*2*).

Several recent experiments (*3*) suggest that recovery of memory after ECS is possible with the aid of a noncontingent "reminder" foot shock (FS) presented between ECS and the retention test. More recently, it was demonstrated that the recovered memory was not due to a change in activity level caused by the interaction of training FS, ECS, and noncontingent "reminder" FS (*4*). Furthermore, these experimenters found that the ability to recover memory was not time dependent, inasmuch as ECS-reminder intervals of 2, 4, 8, 16, 48, and 336 hours all restored memory to a similar degree. Consequently, it appears that ECS may not destroy recently acquired information, but may, instead, interfere with its retrieval.

Similar experiments have observed recovery from cycloheximide-induced amnesia provided the recovery agent was administered within a few hours of training (*5*). Moreover, it was found that the training and recovery stimuli need not be similar, since both amphetamine and corticosteroids were effective in restoring cycloheximide-impaired memories after training with FS. However, both these pharmacological agents were effective in attenuating cycloheximide-induced amnesia only if administered while the short-term memory trace still persisted.

The present experiment was designed to determine whether, as is suggested by "reminder," the training stimulus and the recovery agent must have similar physical properties as well as equivalent internal consequences to produce recovery of memory after ECS. In the present study, stimulus specificity of the recovery agent was investigated by training rats using ice water immersion as the aversive training stimulus (*6*) and using FS as the recovery stimulus. The rationale for training with ice water and "reminding" with FS and not vice versa is that we have found it necessary to manipulate both the intensity and duration of the recovery agent in order to successfully obtain recovery of memory. Inasmuch as it is considerably easier to vary the parameters of FS than those of water, the former was used as the reminder agent and the latter as the training agent.

Subjects for the present experiment were Sprague-Dawley descended, male, albino rats (Carworth Farms) weighing 155 to 180 g at the outset of the experiment. All subjects were individually housed in continuous light and were maintained on 10 g of powdered rat food per day; water was freely available. A two-chambered, V-shaped, step-through device was used for training (*7*). The ceiling and partition between the light and dark compartments were slit to permit suspended and counterweighted wires for delivery of ECS to follow the subject through the gate from one chamber to another. The floor in the dark punishment chamber was hinged and spring-loaded. Activation of a solenoid caused the two parallel metal plates which comprised the floor to swing open. A 30-gal (114-liter) plastic container fitted with an insert was situated directly beneath the apparatus. The insert consisted of a cylinder of sheet metal 30 cm high and 46.5 cm in diameter with an open top and carpenter's cloth screen bottom. The plastic can was partially filled with chopped ice surrounding the insert, and was then filled with tap water to a height of 23 cm above the screen floor and 13 cm below the floor of the step-through apparatus. The temperature of the water was maintained within 2°C of freezing for the entire duration of the experiment. Electroconvulsive shock (54 ma, 60 hertz, 0.3 second) was administered through earclips, while FS (0.25 ma, 60 hertz, 10 seconds) was delivered by a constant-current shock source in an

Table 1. Group mean log latencies and P values for test trial.

Group	N	Mean training trial log latencies (log sec)	Mean test trial log latencies (log sec)	CW + PECS + PFS	CW + ECS + FS	CW + ECS + PFS	NCW + ECS + FS
CW + PECS + FS	16	0.97	1.93	$>.20$	$>.05$	$<.0001$	$<.00001$
CW + PECS + PFS	21	1.09	1.75		$>.20$	$<.001$	$<.001$
CW + ECS + FS	22	0.97	1.65			$<.001$	$<.001$
CW + ECS + PFS	21	1.06	1.16				$>.80$
NCW + ECS +FS	21	1.08	1.13				

operant chamber with a 30 by 30 cm grid floor.

All subjects were fitted with earclips during both training and test trials. After the gate was opened on the training trial, any rat that stepped through in less than 1 second or in more than 30 seconds was replaced, thereby eliminating highly emotional animals. Such rats tend to maintain their characteristic training latencies on the test trial independent of experimental treatment. One group of rats, the basic experimental group, contingent water + ECS + FS (CW + ECS + FS), was placed in the start compartment of the step-through device. On both sets of trials, each rat was placed in the light compartment facing away from the gate separating the two chambers. Three seconds later, the gate was opened, allowing the subjects to enter the punishment chamber. As the subjects entered the punishment chamber, the floor swung open, dropping them into the ice water where they remained for 10 seconds. At this time, while still in the water, they received an ECS. Full tonic-clonic convulsions in the subjects suggested that little current was being shunted through the water. In summary, these animals were punished and received ECS contingent upon emitting a step-through response. This group, like the following groups, was removed to the home cage immediately after ECS.

An amnestic control group, contingent water + ECS + pseudo FS (CW + ECS + PFS), received the identical training procedure as did the CW + ECS + FS group. A third group, contingent water + pseudo ECS + pseudo FS (CW + PECS + PFS), controlling for one-trial passive avoidance of ice water bath, received the same training as the CW + ECS + FS and CW + ECS + PFS groups except that they received pseudo ECS. These rats were returned to the home cage after spending 10.3 seconds in the ice water with earclips affixed. A fourth group was included to evaluate the additive affects of training with ice water and the noncontingent FS. This group, CW + PECS + FS, was immersed in the ice water following the step-through response and received pseudo ECS.

In order to assess the interaction of the experimental treatments (water, ECS, and FS) that could conceivably produce alterations in activity level during the test trial, a fifth group, noncontingent water + ECS + FS (NCW + ECS + FS), was given an unpunished step-through trial. Although it was unnecessary to expose this group to the step-through apparatus prior to testing in order to control for changes in activity level, this procedure served to permit elimination of extremely fast or slow subjects. One hour after the unpunished step-through response these animals had earclips affixed and were simply dropped from the experimenter's hand into a container of ice water. Ten seconds later, while still in the water, a transpinnate ECS was delivered. Throughout the training of all five groups the experimenter wore a white coat and cloth gloves.

Two hours subsequent to being dropped into the ice water, all subjects were placed in the operant chamber. After 30 seconds, the CW + PECS + FS, NCW + ECS +FS, and CW + ECS + FS groups were given a 10-second FS, while the CW + PECS + PFS and CW + ECS + PFS groups received pseudo FS (40 seconds in operant chamber without receiving FS). A black rubber apron and leather gloves were worn by the experimenter during this phase of the experiment in contrast to the white cloth coat and cloth gloves used during training and test trials. This change of garb was designed to minimize generalization of fear to the step-through device which might have been induced by the noncontingent FS.

Retention testing was conducted 24 hours after training and was performed "blind." Each subject was placed in the start chamber of the step-through device facing away from the gate. Three seconds later the gate was opened and step-through latencies were recorded. Test trials were terminated if the subject remained in the start chamber for 300 seconds. Log transformations of both training and test trial latencies were performed to permit parametric statistical analysis.

Inspection of test trial latencies revealed that the CW + ECS + FS, CW + PECS + FS, and CW + PECS + PFS groups evidenced comparable step-through latencies as did the CW + ECS + PFS and NCW + ECS + FS groups. An analysis of variance performed on training trial log latencies proved to be nonsignificant ($P > .5$) and was consistent with the hypothesis that there were no pretreatment differences between groups. A similar one-way analysis of test trial log latencies proved to be significant ($P < .001$). Individual two-tailed t-tests were performed between all five groups; Table 1 summarizes the results of these tests. A 2×2 analysis of variance on the test trial log latencies of the CW + ECS + FS, CW + ECS + PFS, CW + PECS + FS, and CW + PECS + PFS groups found that the ECS and FS effects were significant ($P < .025$, $P < .005$) while the interaction was not significant ($P > .10$). The significant FS effect and nonsignificant FS $\times$ ECS interaction suggests that noncontingent FS may serve to elevate the latency of any subject regardless of treatment. Alternatively, FS may serve both to induce recovery from amnesia and to elevate the latencies of the CW + PECS + FS group (perhaps counteracting a small degree of spontaneous decay of memory). However, the low latencies of the NCW + ECS + FS group indicates the latter explanation to be correct.

The comparably long latencies of the CW + PECS + PFS and CW + PECS + FS groups demonstrate that ice water can produce one-trial passive avoidance and that noncontingent FS does not significantly affect the latencies of rats trained with ice water. The relatively

short latencies of the CW + ECS + PFS group are consistent with the previously reported ECS-induced amnesia for this task (*8*). The potential of noncontingent FS to induce recovery of memory of ice water is demonstrated by the CW + ECS + FS group. The long latencies evident in this group suggest that amnesia was largely, if not totally, reversed. Such data support the hypothesis that ECS hampers retrieval but does not destroy the memory of recently learned information. Furthermore, the return of memory was specific to the training situation and not merely a change in activity level. Lack of avoidance in the NCW + ECS + FS group demonstrates that the long latencies of the CW + ECS + FS group were not a function of a reduction in mobility level due to the interaction of ice water, ECS, and FS.

Inhibition of the step-through response by the CW + ECS + FS group indicates that noncontingent FS has reactivated a retrieval mechanism for memory of training with ice water. This study, as well as others which have reversed the amnestic effects of ECS or cycloheximide, indicate that at least these two amnestic agents interfere with retrieval mechanisms rather than, or in addition to, disrupting storage processes. Alternative interpretations of experimental amnesia produced by ECS ordinarily invoke a consolidation (storage) impairment model in which information is either prevented from entering long-term storage or is stored in a degraded form. However, such a model cannot explain reversal of amnesia induced by a noncontingent recovery agent which was quite dissimilar from any stimulus present during the training trial. As relevant information was not available during the recovery event, any memory present at the time of testing must have been previously present but unavailable. Regardless of the quality of the memory that is stored following ECS, it is nevertheless apparent that ECS disrupts retrieval of such memories rather than completely blocking their storage. Moreover, it is difficult to support the assumption that ECS ever prevents or distorts the storage of recently acquired information on the basis of present data. Recovery from experimental amnesia is clear evidence for retrieval failure, whereas a failure to reverse amnesia is not unambiguous proof of a consolidation impairment. Inability to produce recovery of memory following ECS is always potentially a function of using inappropriate recovery agent parameters. Conclusive evidence of a consolidation failure requires that the specific structural form of a memory be identified in trained animals as well as being found absent in amnestic animals.

The reversal of amnesia produced in the present experiment using different training and recovery stimuli parallels the reversal of cycloheximide-induced amnesia (*5*). Previous reports of recovery from ECS-induced amnesia has tended to refer to the recovery agent as a "reminder" (*4*). A cognitively oriented model underlying the term "reminder" assumes that specific features of the recovery agent reactivate memories of prior events similar to the recovery event, explicitly, those of training. Consequently, noncontingent FS was previously used to remind amnestic animals of prior training with FS (*3, 4*). The present data require a revision in the concept of "reminder," since noncontingent FS assumedly possesses few physical properties in common with ice water and is yet able to restore memory of prior training with ice water. These data should not be misconstrued as suggesting that the recovery agent can be totally dissimilar from the training event and yet be able to induce recovery of memory. Instead, FS may effectively restore memory of training with ice water because these two agents have similar arousal properties. This explanation is in effect a generalization of the "reminder" position, and is consistent with the recovery of FS memories from cycloheximide-induced amnesia achieved with amphetamine and corticosteroids (*5*).

Because of the gross neural discharges triggered by ECS, it is most improbable that any information uniquely encoded in the format of electrochemical transmission survives the neural seizure. Therefore, information retained after ECS must necessarily be at least partially encoded in a less vulnerable form than neural transmission. In the present experiment ECS onset followed initial contact with ice water by 10 seconds. Since memory of training proved recoverable, this interval defines a maximal consolidation time necessary for one-trial passive avoidance of ice water immersion. Moreover, this brief interval is consistent with the less than 500 msec consolidation interval previously reported in a study using a familiarization paradigm (*9*).

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Axonal Transport of Gangliosides in the Goldfish Optic Nerve

Abstract. *Radioactive glucosamine and* N*-acetylmannosamine injected into the goldfish eye are incorporated into gangliosides that undergo rapid axonal transport to the optic nerve terminals. All ganglioside fractions are labeled. These data provide the first evidence that axonal transport has a role in neuronal ganglioside function and metabolism.*

The brain contains a high concentration of ganglioside compared to other tissues (*1*) and appears to be the only organ with more of its sialic acid in lipid-bound form (that is, in ganglioside) than in glycoprotein (*2*). Gangliosides occur at low concentrations in isolated astrocytes (*3*), oligodendroglia (*4*), neuronal perikarya (*3*), and myelin (*5*), while in contrast they show considerable enrichment in the synaptosomal and microsomal fractions (*6*). The source of nerve-ending ganglioside poses an intriguing and still unsolved problem. Local synthesis is one possibility in view of evidence for the presence of glycosyltransferase enzymes in synaptosomal fractions (*7*). However, cell-body syn-