1972

Transfer of FR Response Rate Bias to FI Trained Guinea Pigs by Injection of Brain Homogenate

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TRANSFER OF FR RESPONSE RATE BIAS TO FI TRAINED
GUINEA PIGS BY INJECTION OF BRAIN HOMOGENATE

by

Lief Carlsen

SENIOR HONORS THESIS

Approved:

UTAH STATE UNIVERSITY
Logan, Utah
1972
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INTRODUCTION

Origin and nature of problem

In an attempt to delineate the physiological and/or chemical nature of the memory process, some researchers have reported that by introducing all or part of the brain of a trained animal into the bloodstream of another animal, the recipient thereby "acquires a tendency" to respond as the donor was trained (Fjerdingstad, Nissen, and Roigaard-Petersen, 1965; Nissen, Roigaard-Petersen and Fjerdingstad, 1965; Babich, Jacobson and Bubash, 1965; Ungar and Oceguera-Navarro, 1965). However, almost as many researchers have failed to obtain significant results (Gross and Carey 1965; Luttges et al., 1966; Halas et al., 1966; Branch and Viney, 1966).

Because many of the early experiments had less than optimum designs, their results were often equivocal. Critics frequently pointed out that perhaps increased learning efficiency was due merely to a sensitizing or stimulating effect of the injection and not to any specific transfer of learning. It was in an attempt to answer this criticism that the following experiment was performed.

Objectives

1. To show a transfer of learning while controlling for stimulating or depressing effects of brain homogenate.

2. To show, specifically, that fixed ratio (FR) shock escape behavior can be transferred to an animal trained on fixed interval (FI) shock escape.
Rationale

If the brain homogenate has merely a sensitizing or stimulating effect, specific donor training should have no effect on subsequent recipient behavior. Conversely, if a recipient can be shown to respond differently on a task to two injections from animals trained differently on the same task, the recipient’s behavior may be assumed to be due to the differences in specific donor training.

Summary of procedure

I attempted to demonstrate these objectives in my experiment by training two guinea pigs to respond in the presence of electric foot shock at a low rate by training them on a sixty second, fixed-interval schedule of shock escape (FI 60”). In such a schedule any bar press response made by the animal during the first sixty seconds after the shock is turned on has no programmed consequences. The first response made after the sixty seconds have elapsed turns the shock off for ten seconds. Following the ten seconds of shock off the cycle repeats itself. Such sessions lasted one hour. On such a schedule, animals typically learn to emit very few responses per hour in as much as the most efficient rate would be one per minute. The two subjects trained with this schedule were to receive the homogenated brains of two subjects trained to respond at a high rate in the presence of electric shock. These guinea pigs (trained donors) were trained on a fixed ratio of twenty (FR 20) whereby the shock was turned off as soon as the animal pressed the bar twenty times. Typically, animals in this
situation learn to respond by immediately pressing the bar "as fast as they can" and consequently amass many times the total number of responses per hour that animals on FI produce.

When both donors and recipients were responding in a stable manner to the shock, the homogenated brains of two pigs with no training were to be injected into the low rate responders (FI trained) as control injections to determine if brain homogenate per se acted as either a depressant or stimulant. It was presumed that the naive injection would have either a slight depressing or no detectable effect on the FI trained recipient animals. The homogenated brains of the FR donor animals would subsequently be injected into the FI recipient animals. If the response rate of the FI animals increased significantly only after FR donor brain homogenate injection, it could safely be attributed to the training of the FR animals. Transfer of response rate learning could then be said to have occurred.
Planarian studies

In 1959, McConnell, Jacobsen, and Kimble found that planaria classically conditioned to a specific stimulus could be bisected an both halves, when allowed to regenerate, showed retention equal to that of uncut controls. McConnell (1962) went on to find that if a trained planarian is chopped up and fed to another untrained planarian, the cannibal learns the test task much faster than controls.

Suspicious of what McConnell had accepted as a "conditioned planarian", James and Halas (1964) attempted to determine whether actual conditioning occurred using the McConnell paradigm through the use of resistance to extinction as an index of learning. They concluded that no real conditioning could be shown to occur in planaria and therefore ruled out McConnell's claim that transfer of learning had occurred. Jacobsen, Horowitz and Fried, (1962), in a study which attempted to control for sensitization and pseudoconditioning, presented evidence strongly in favor of true conditioning. Thus the question of inter-planarian transfer of learning may still be debatable.

RNA extraction studies

McConnell's work raised the interesting possibility that inter-animal transfer of learning might exist in higher animals. Because considerable evidence had been compiled suggesting RNA (ribonucleic acid) played an important role in memory, early investigators in this area extracted RNA from the brains of trained rats and injected it into
naive recipients (Fjerdingstad, Nissen and Roigaard-Petersen, 1965). Those rats injected with "trained RNA" were found to learn significantly faster than controls. Jacobsen et al., (1965, 1966) performed a series of studies using RNA extracts and claimed that transfer was shown in all experiments. These experiments were strongly criticized by Carney (1965), Barker (1966), and Worthington and Macmillan (1966) among others, on the grounds of faulty methodology. Replication studies done after Jacobsen's and Fjerdingstad's studies have reported negative results (Corson and Enesco, 1966; Gross and Carey, 1965; Luttges et al., 1966; Halas et al. 1966; Branch and Viney, 1966).

**Brain homogenate studies**

Suspecting that the RNA extraction procedure might have a deleterious effect on positive transfer, Ungar and Oceguera-Navarro, 1965) used whole brain homogenate for their injections. Recipients of trained brain reached criterion performance in 1.25 days as compared with 12.0 days for controls. Numerous others have since reported transfer using brain homogenate (Byrne and Samuel, 1966; Byrne and Hughes, 1967; Krech, Bennett and Ragan, 1967). In none of these experiments, however, can sensitization be ruled out.
METHOD

Subjects
Six adult male guinea pigs served. All were approximately the same weight. Five were less than six months old and had no previous training prior to this experiment. One of the recipients was two years old and had previously been trained on an FI schedule. Subjects were housed in individual 10" x 12" x 10" wire mesh cages when not in the experimental apparatus. Food and water was removed from the home cages one hour prior to running time each day.

Apparatus
A typical small animal chamber (Skinner box) with grid-rod floor and lever operandum was the experimental space. Shock was supplied from a commercial shock generator/scrambler such that polarity on each rod changed many times a second. Shock level was individually determined for each animal in terms of milliamps required for consistent performance.

Procedure

FI 60" recipients. The two guinea pigs trained as recipients were run for three weeks on a fixed-interval, sixty second shock escape schedule. Reinforcement was ten seconds of time out from electric shock.

Naive donors. These guinea pigs were placed in the training apparatus for one hour each day but received no shock or other programmed stimulation during this time. Bar pressing responses were recorded to obtain operant levels.
FR 20 donors. These two animals were trained for five sessions by gradually increasing the number of responses required to terminate shock until the number twenty was reached. For the remaining two weeks of training they remained on a FR 20 schedule with ten seconds time out for each twenty responses.

The sequence for recipient injections was first naive, then five sessions, then FR 20, then five more sessions. Stability on the FI schedule was reached prior to the first injection and was reestablished prior to the second injection.

When recipients showed satisfactory stable rates, the naive donors were decapitated, their brains removed in less than two minutes, rinsed in cold normal saline and stored on dry ice for 24 hours prior to injection (McConnell et al, 1970). Two hours and fifteen minutes prior to the usual running time of the recipients, the two donor brains were homogenized together in a hand-held grinder with two cc of cold sterile saline. The homogenizing was accomplished while the grinder was held in an ice bath and required no more than ten minutes. Additional cold saline was added to the homogenate to provide five to eight cc of injectable medium. Injections proceeded as described above and the recipient animal was returned to his home cage. Two hours later the normal FI 60" session was run. There has been a report (Schad, Rollins, and Snyder, 1969) suggesting differential effects as a function of time between injection and test. Since baseline was recovered between sessions, the recipients in the present experiment were run 24 hours, 50 hours and so on after each injection.
Each recipient received two injections; one consisting of one-half of the two combined brains from naive donors and one of one-half of the two combined brains from the FR 20 donors. The sequence of injections and the day of injection were the same for both recipients. Previous response rate stability was regained between injections and no injections were given within five calendar days of another.
RESULTS

All of the trained subjects achieved criterion on their respective schedules. The mean number of bar presses per hour for the FI 60" recipients, nontreated was 150. Mean response rate of the FR 20 donors for five sessions prior to sacrifice was 1320 per hour. Mean operant level for the naive donors was two responses per hour. Cumulative records of the trained animals' sessions indicated the typical shape expected from these schedules (Ferster and Skinner, 1957).

Two hours after injection of naive homogenate the recipients' rate showed no significant change from pre-injection rate. The animals were run again at 24 hours post-injection and each day thereafter for five days. There was no significant change in their rates.

Five days after the first injection the same two recipient FI animals were injected with FR 20 trained brain homogenate. Two hours following this injection they were run on their usual FI 60" schedule. One animal (B) (the older and previously trained one) showed no significant change in response rate. When tested again for the next five days he continued to respond at the same slow rate as before the injection. The cumulative response records of this animal are shown in Figure 2. The other recipient (A) showed nearly a 300% increase in response rate two hours after the injection (325/hr compared with 1250/hr). When he was run 24 hours after the injection his rate had risen to 2566/hour. 36 hours after the injection the rate was 4990/hour (a 1400% increase over pre-injection rate and three times that of the FR 20 donors!). One week after injection his rate was 3095/hour. The cumulative response records of this animal are shown in Figure 1.
Figure 1. Comparison of pre and post-injection response rates in recipient
A. $A =$ nontreated rate; $B =$ post naive injection rate; $C =$ post FR injection rate.
Figure 2. Comparison of pre and post-injection response rates in recipient B. A = nontreated rate; B = post naive injection rate; C = post FR injection rate.
DISCUSSION AND CONCLUSIONS

Because of the small number of subjects used in this experiment, it would be almost impossible to show unquestionable results. This weakness in experimental design does not reflect improvidence, rather the frugality of an underfinanced psychology laboratory. Bearing this in mind, the results are equivocal.

As predicted, injections of naive brain had no effect on response rate with either recipient. This would indicate that brain homogenate per se is neither a stimulant nor a depressant. The effect of the injections on performance therefore, must be due to some specific factor of the brain homogenate that can in fact be transferred from one animal to another.

While one recipient (A) showed a dramatic behavioral change after the experimental FR trained injection, the other recipient (B) showed none. If indeed the phenomenon under study is real, I offer the following as a possible explanation for the failure of the one recipient to respond as predicted. The nonreactor was an older animal than the other one and had been used in numerous other experiments of a different nature. He had for some extended period of time (10 - 12 months) maintained a stable FI rate prior to my use of him. It is possible that the sheer tenacity of such a long established behavior is much more difficult to modify and thus the injection did not have the effect on him it did on a more recently trained animal. The overtrained brain may also be less susceptible to this kind of treatment. Sidman (1960) indicates the very real nature of "locked rate" performance wherein performance is not modifiable by drastic manipulation in the program.
Recipient A's overly high rate of responding following the FR injection is also somewhat disconcerting. The donors in this case had been responding at an average of 1300 responses per hour. Why should such brain homogenate when injected into another animal result in response rates of 4990 per hour? It seems to be a case of an effect with insufficient cause. My only explanation is that the recipient did in fact change his response topography from the usual "front paw on bar" to "chattering" the bar between his teeth during the experimental session. The chatter method of responding typically results in very high rates. Neither of his donors chattered. The critical point however is that no change occurred after naive injections but it did after trained injections. This is not very convincing but it suggests that this line of inquiry deserves further research.

In summary, the evidence from many labs is positive yet there is a good deal of failure also reported. My experiment was admittedly small in scope and objectives, yet I feel that I benefited from it in terms of laboratory experience and scientific writing technique.


James, R.L. and E.S. Halas. 1964. No difference in extinction behavior in planaria following various types and amounts of training. Psychol. Rec. 14: 1-11


