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by

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Running Head: Enriched Rats

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Hebb's (1949) The organization of behavior. started an entire field of research examining the effect of environmental factors on brain development. The bulk of these studies have indicated a significant beneficial effect of enriched environmental conditions (EC) upon recovery of function, brain morphology and chemistry, and learning. Many current practical applications had their conceptions based on studies of EC. Replacement of cages with natural environment enclosures for zoo animals was founded by Markowitz (1982) on the premise of benefits from EC. Using EC rather than impoverished conditions (IC) in the raising of farm animals caused increased growth and decreased aggression (Wood-Gush, Stolba, & Miller, 1983). Bennet and Rosenzweig (1981) had suggested using enrichment on all lab animals prior to experimental use so that the results would be more representative of the natural species. This research has also started such programs as the "foster grand-parent" program to help keep the elderly mentally fit (Sandman & Donnelly, 1983) and programs to promote mental and social development in Down Syndrome children (Hayden & Haring, 1985). Differences between individuals, ethnic groups, social classes, and geographical areas on measures of intelligence, learning, and memory might be eliminated or reduced by increasing the degree of enrichment in underdeveloped schools and neighborhoods.

Enrichment Subjects

Research has shown the positive effects of EC are universal across subject groups. Although there might be sex differences in EC effects, these effects have been shown to occur in both sexes (Juraska, 1984; Juraska, Fitch, Henderson, & Rivers, 1985; Loy & Milner, 1980; Milner & Loy, 1980). Enrichment effects were also found to occur during several periods throughout the lifespan (Diamond, 1967; Diamond, Johnson, Protti, Ott, & Kajisa, 1985; Greenough, Volkmar, & Juraska, 1973; Malkasian & Diamond, 1971). The effects of environmental enrichment have been demonstrated in many species including rats, squirrels, monkeys, dogs, and humans (Floeter & Greenough, 1979; Hayden & Haring, 1985; La Torre, 1968; Rosenzweig & Bennet, 1969; Rosenzweig, Bennet, Alberti, Morimoto, & Renner, 1982; Rosenzweig, Bennet, Alberti, & Renner, 1982; Zimbardo & Montgomery, 1957).

Recovery of Function

Enrichment has influenced the ability of subjects to regain the loss of their mental functions due to brain surgery. Numerous studies reported benefits on recovery in rats given postsurgical EC experiences (Bartus, Flicker, Dean, Pontecorvo, Figueiredo, & Fisher, 1985; Bartus, Pontecorvo, Flicker, Dean, & Figueiredo, 1986; Gentile, Beheshti, & Held, 1987; Greenough, Fass, & De Voogd, 1976; Held, Gordon, & Gentile, 1985; Schwartz, 1964; Will, Rosenzweig, & Bennet, 1976; Will, Rosenzweig, Bennet, Hebert, & Morimoto, 1977). Preoperative exposure to EC was found to aid in minimizing the loss of function (Gentile, Behesti, & Held, 1987; Held, Gordon, & Gentile, 1985; Hughes, 1965; Smith,

1959). Various brain structures have been lesioned to test the regaining of abilities with EC experience. Tests upon the hippocampus (Einon, Morgan, & Will, 1980), septum (Donovick, Burright, & Swidler, 1973), visual cortex (Schwartz, 1964; Will et al., 1976; Will et al., 1977), sensorimotor cortex (Gentile et al., 1987, Held et al., 1985), and even hemidecortication (Whishaw, Zaborowski, & Kolb, 1984) produced successful results. The dynamic changes in brain morphology and chemistry produced by enrichment possibly were the causal factors in the recovery of function.

Neurological Changes

The brains of animal subjects undergo significant changes from EC experience. Not only were brain weights found to increase with enrichment (Diamond, 1967; Diamond, Rosenzweig, Bennet, Lindner, & Lyon, 1972; Reige, 1971; Rosenzweig, Bennet, & Diamond, 1972), but the increases persisted even after a subsequent month of IC (Katz & Davies, 1984). Rosenzweig, Krech, Bennet, & Diamond (1962) reported a consistent 3.3% average increase in somatosensory cortex weight and a 7.6% average increase in the weight of visual cortex after EC. Increases in cortical size have been documented in EC research (Diamond et al., 1985; Diamond, Krech, & Rosenzweig, 1964; Diamond, Law, Rhodes, Lindner, Rosenzweig, Krech, & Bennet, 1966; Diamond, Lindner, & Raymond, 1967; Diamond, et al., 1972).

Researchers identified alterations in neurons and other cellular structures. Many of these changes involved dendrites (Greenough & Volkmar, 1973; Juraska et al., 1985). In comparison with IC animals, EC animals had more extensive dentritic

branching (Fiala, Joyce, & Greenough, 1978; Greenough & Volkmar, 1973) that was able to persist through 30 days of IC following the EC exposure (Camel, Withers, & Greenough, 1986). Dendrites were also found in visual cortex to be longer in length (Conner, Melone, Yuen, & Diamond, 1981; Conner, Wang, & Diamond, 1982; Greenough & Volkmar, 1973; Turner & Greenough, 1985; Uylings, Kuypers, Diamond, & Veltman, 1978). Changes have been reported in the number and size of neuronal cell bodies (Diamond, Johnson, Ingham, Rosenzweig, & Bennet, 1975; Diamond et al., 1967). Studies also showed EC increases in measures of glial cell density (Altman & Das, 1964; Diamond et al., 1966).

Enriched conditions appeared to produce biochemical, physiological, and anatomical changes which could be interpreted as improved synaptic transmission. Diamond, Johnson, and Ingham (1975) documented alterations in synaptic clefts. Cholinesterase and acetylcholinesterase have been linked to synaptic transmission, and both increases and decreases in the level per unit of brain tissue of these substances were found following EC (Bennet, Krech, & Rosenzweig, 1963; Bennet & Rosenzweig, 1971; Diamond, Krech, & Rosenzweig, 1964; Rosenzweig & Bennet, 1969). Electrophysiological augmentation of synaptic transmission was demonstrated from EC in the hippocampal system. These studies found that electrical stimulation of the primary afferent input to the dentate gyrus cells of the hippocampus (i.e., the perforant path) in EC animals gave a larger excitatory postsynaptic potential as well as an increase in the size of the population spike (i.e., indicative of the number of neurons responding (Green & Greenough, 1986; Sharp, McNaughton,

& Barnes, 1985).

After EC, the number of larger cranial blood vessels and vascular capacity in the brain had increased significantly (Diamond et al., 1964; Black, Sirevaag, & Greenough; 1987). Bennet and Rosenzweig (1971) showed improved incorporation of amino acids, larger amounts of DNA, and RNA with more complex sequence diversity (Grouse, Schrier, Bennet, Rosenzweig, & Nelson, 1978). These parameters might have resulted from the need for a greater metabolic rate to support increased neurotransmission.

Learning Enhancement

These neuroanatomical changes generated by enrichment have provided a biological basis to support the findings on EC and learning enhancement. Research of EC effect on learning has produced rats with greater problem-solving abilities and performance on various learning tasks (Bingham & Griffiths, 1952; Eingold, 1956; Forgays & Forgays, 1952; Forgus, 1956; Greenough, 1976; Hebb, 1947; Hebb, 1949; Hebb & Williams, 1946; Hymovitch, 1952; Meier & McGee, 1959). Visual exposure to simple geometric shapes aided animals in reaching criteria faster and making fewer errors (Gibson & Walk, 1956). The benefit to learning from enrichment was found to persist after EC was stopped and animals were switched to IC for some time (Forgays & Read, 1962; Greenough, Madden, & Fleischmann, 1972; Hymovitch, 1952). The results of the Gibson and Walk (1956) study were expanded upon by Hall (1979) when he tested the learning benefits from both early and late enrichment on rats. The two age groups could perform equally on a visual

discrimination task and both groups were significantly better than the IC control rats.

One of the best illustrations of EC benefits was done by Bartus and associates (1985, 1986). Rats which had been given bilateral lesions of the nucleus basalis magnocellularis and kept in IC postsurgically for 6 months displayed an impairment in learning of a passive avoidance task (Bartus et al., 1986). However, rats undergoing the same surgery but spending 6 months learning a radial arm maze task had no deficiencies in learning the same passive avoidance task (Bartus et al., 1985).

The greater sensory stimulation of enriched conditions appeared to be the causal factor of both the neuroanatomical changes and learning facilitation. This idea has been supported by two studies. Forgays and Forgays (1952) showed animals from an EC with toys outperformed animals from an EC without toys on the Hebb-Williams (1946) intelligence test and Rabinovitch (1949) closed field test. Further, research subjects given only visual experience of EC toys were inferior in visual discrimination ability to subjects given both tactile and visual exposure (Meier & McGee, 1959).

Hippocampal Involvement

Fiala, Joyce, and Greenough (1978) cited several studies that indicated animals with hippocampal damage performed similarly to IC animals with respect to EC animals. A recent study by Markowska and Olton (1988) found rats with fimbria-fornix damage were unable to execute above chance on a delayed-match-to-sample (DMTS) visual discrimination task with three dimensional objects in a water maze, but control animals could

achieve an accuracy rate of 80%. The DMTS and the delayed-nonmatch-to-sample (DNMTS) visual discrimination tasks have been used to test working memory in primates and humans (Aggleton, 1985). The DMTS/DNMTS discrimination tasks showed sensitivity to memory deficits in humans and monkeys (personal communication, Dr. D. Smith). Working memory (Hirsch, 1974; Hirsch & Leber, 1978) and environmental orientation (O'Keefe & Nadel, 1978) have been considered functions of the hippocampus. Damage to this brain structure produced learning deficits, and the alterations produced by EC to the hippocampus seemed at least partly responsible for the increased learning ability (Einon et al., 1980; Green & Greenough, 1986; Sharp et al., 1985). Rats have also been successfully trained on the DMTS/DNMTS task (Aggleton, 1985; Markowska & Olton, 1988; Alexinsky & Chapouthier, 1978; Olton & Feustle, 1981).

Contrary Evidence

Some research findings have been contradictive to the EC effects. Rearing of animals in differential environments in certain studies had no effect upon the ability of the animal to learn (Gill, Reid, & Porter, 1966; Hughes, 1965; Ough, Beatty, & Khalili, 1972). More interesting were accounts of subjects raised in IC that performed better than their EC counterparts learning (Bennet, Rosenzweig, & Diamond, 1970; Coburn & Tarte, 1976; Lamden & Rose, 1979). Considering the lack of a standardized EC and that enrichment is only a relative term, the difference between enrichment methodologies could have caused contradictory findings in some of the research. The results might have been affected by variations in plasticity of different

neurological structures being specifically tested by the various tasks. A strain of abnormally dull rats or other subjects may have confounded some of the studies as well.

Hypothesis

This study was an attempt to show that enriched rats can learn a three dimensional object visual discrimination DMTS and DNMTS task. The task utilized toys from the EC for sample objects on an alternating arm Y-maze. Any subjects which were successful in learning the task were to then be tested as to the the effects of reversible inactivation of the hippocampus on the performance of these tasks.

METHOD

Subjects

Subjects were 12 male Long-Evans hooded rats obtained from local breeding stock. The subjects were weaned at thirty days and housed in groups of three to four littermates in clear plastic cages. The animal room environment was a 12-hr diurnal light cycle with food and water ad libitum.

Apparatus and Materials

The enriched environment was a 40x40x8 inch wood, open field maze. The interior of the box had been painted grey with the floor subdivided by 1/4 inch white stripes into 16 quadrants. A 40x41x2 inch wood frame covered by cooper wire mesh was placed on top of the maze to keep the rats inside the EC box.

Three metal rods were placed diagonally across the box's top in order to suspend 10 toys by wire. A pool of thirty objects of various sizes, shapes, colors, and materials had been

collected for placement inside the box to constitute the EC. Examples of objects used were a coffee can, a golf ball, and a Stomper 4x4 (trademark) mountain playset. Another fifty toys were collected for use as the novel objects which the subjects were not exposed to either during the enrichment period or during the time in which was permitted to observe the training task sample object.

An elevated Y-maze was used as the training apparatus for the DNMTS/DMTS tasks. The start box was a 6x6x6 inch white plexiglass box attached to a sideways U-shaped doorway that allowed doors to slide in and out from the righthand side. The connector box was an A-shaped plexiglass box with a white floor, black sides, and a clear hinged top. The arms were 6x30x6 with black plexiglass sides, white hinged top, and an open bottom with metal rods spaced 1/2 inch apart for a walking surface. Two inch diameter tin trays had been secured to the floor rods 20 inches inside the arms for the reward containers. The platform on which the Y-maze sat was V-shaped with each arm being 16x48 planks on 7 inch high wood legs.

Procedures

Enrichment

At thirty days of age, a litter was placed into the EC for a 3-hr period at 4:00 or 7:00 pm daily. The ten suspended toys were randomly assigned to one of the rods for a week and the rods rotated both in position and direction daily to insure that the rats had maximal experience with all objects. A number of the thirty extra objects would be placed into the EC weekly. The environment of the EC room had to be altered in order to increase

subjects' activity level. Alterations included lowering the light intensity, raising room temperature, and using a white noise generator.

Deprivation

The subjects were weighed on the last three days of EC to determine their average body weight. The rats were then put on a 23-hr food deprivation schedule to maintain them at 90% of their average body weight. The appropriate amount of food provided daily was determined by their pre-training weight and administered after training in their food containers.

Training

The rats started training on the final week of the 90 days of enrichment by being placed into the Y-maze for 10 minutes daily so they could become habituated to the apparatus. Then the rats were randomly assigned to one of three trainers and one of two training conditions: DMTS or DNMTS. The first two weeks of training consisted of a 5 trials per day schedule that was increased to 7 trials per day for the following two week period. Starting the fifth week of training, rats were trained on 10 trials per day until they reached a criteria which was established as performing at or above 80% correct for more than seven days in a row.

The trials were a random alternating arm match or nonmatch-to-sample task with a short delay. Ten of the suspended EC toys served as the sample objects. A pool of fifty toys the subjects had never been exposed to were divided into five groups so that each group of 10 novel objects would only be seen by the rats every fifth week. The alternating schedule and pairing of novel

to sample toys was done in advance for each weekly trial period.

Each trial began with the placing of the rat into the start box. The trainer slid an opaque door aside so the subject would see the sample. Once the subject had looked in the direction of the sample for 5 seconds, the white door was slid back into its original position so the rats were not able to see the placement of the objects at the maze arm openings. After 5 seconds, both the white and clear doors were pulled aside allowing the subject access to the connector box and the maze arms. Self-correction was used during the first four weeks of training. Letting the animal go into the correct arm after choosing the wrong arm was used in an attempt to increase the rate of learning. A subject making a correct response recieved a quarter of a Fruit Loop (trademark) which had been placed into the tray of the correct arm. In the DMTS task, the rat was to choose the arm which contained the sample object within its entrance. For the DNMTS task, the entrance having the novel object in its entrance was the correct choice for the rat. All four rats of a trainer had to complete a given trial before the next trial was administered. The subjects were returned to their cages and fed upon completion of that day's trials.

Surgery

Once a subject had reached criteria, the animal underwent stereotaxic surgery in order to bilaterally implant 14-mm long 23 gauge cannulae to the hippocampus. The subject received a 50-mg/kg injection of pentobarbital for anesthesia. Coordinates for cannulea were based on the Pelligrino Atlas and the nose bar at 5-mm above horizontal. The anterior/posterior (AP) and

dorsal/ventral (DV) positions were set from ear bar zero, and the medial/lateral (ML) aspect was found from bregma. The stereotaxic coordinates used were -1.8 AP, +5.0 DV, and -4.5 ML. Cannulea and securing screws were be held onto the skull with dental cement. A week of postsurgical rest would be given to recover from the operation. After recovery, subjects were be retrained until they achieved criteria on the same task again.

Inactivation

Testing animals on the effects of inactivating a brain structure usually required half of the subjects to have the structure destroyed by lesioning while the other rats served as controls. Lidocaine is a known sodium channel blocking agent that prevents the movement of sodium ions into the neuron for the generation of action potentials necessary for synaptic transmission. Thus the brain structure can be temporarily inactivated accomplishing the same effect as lesioning, but the subject becomes normal after metabolism of the drug in 30-minutes. This technique allows each subject to serve in both experimental and control conditions (personal communication, Dr. D. Smith).

Testing

The test for this experiment was the same DMTS/DNMTS visual discrimination task on which the rats were trained. Subjects were to perform the task in each of the following conditions: baseline (prelidocaine), during inactivation, and postlidocaine (24-hrs later). A repeated measures within subjects ANOVA was then to be used for statistical analysis.

RESULTS

After the fourteenth week of training, the decision was made to alter the experiment's procedures.

Insert figures M1-M6 and N1-N6

The subjects average weekly performance rate had clearly reached asymptote which was below the arbitrarily criteria. The researcher went through the weekly pairings of novel to sample objects during the previous month and found object pairs which the subjects had accurately choosen at near 100% and other pairs that were well below chance in accuracy rate. The problem in acheiving criteria on the task seemed to be caused by pairs of objects the subjects were incapable of discriminating visually. So the researcher selected those pairs that the subjects had correctly choosen with an accuracy rate of at least 80%. These 10 pairs were used for the remainder of the experiment. Each pair was randomly assigned to trial order and to which object of the pair would be used for the sample during a week. The subjects were also allowed 15 seconds to view the sample in case the visual system of the rat required more time to process complex stimulus.

Only one subject reached criteria after nineteen weeks of training (see table M5). After the twentyfourth week, no other subjects were close to achieving criteria so the training was stopped (see tables M1-6 and N1-6). The one rat was operated on successfully and recovered quickly during the following week. The subject has not yet reached criteria so that the second part

of the study can be completed.

DISCUSSION

This study has produced conflicting results in that one rat could successfully complete training. The differences between litters, trainers, and tasks could have caused certain rats to perform better than the others. Although possible, these factors would have influenced groups of rats rather than an individual rat and no such effects appeared in the data.

The enriched environment was one of the more likely elements that would have influenced the rats ability to perform on the task. A rat could have received a greater amount of enrichment than the others according to the extent of exploration early in the EC period. Room conditions did have to be altered after two weeks of EC to increase subjects activity. The duration of enrichment both in terms of daily exposure and number of days might have influenced the rats' neuroanatomical and cognitive development. An inadequate amount of sensory or learning stimulation from the EC may have been another factor.

The rats' visual system has limitations which probably makes the discrimination of objects very difficult. Specifically, in order for the three-dimensional aspects of a stimulus to be perceived, the object has to be within the rat's narrow (i.e., ten degrees) binocular visual field. If the sample or stimulus was not in this part of the visual field, the subjects would be attempting to solve a complex two-dimensional visual discrimination and this seemed to be the problem encountered in this study. Since no means of determining what the rats were looking at was possible, only an indirect measure

of the head toward the sample object could be obtained. This influence was a definite factor in the first part of the training. While all ten pairs used in the second stage of the training had an average accuracy rate over 80%, the average accuracy for all the pairs by all twelve rats had decreased to 60% at the end of the twentyfourth week. A reason for the decrease in accuracy rate may have been due to confusion from the constant switching of sample to novel. Food deprivation has a questionable level of motivation when compared to the motivation level in a water maze as used by Markowska and Olton (1988). Those authors had the objects suspended much higher above the rat than in the present study also.

Even though the one rat was able to perform over the 80% accuracy level for more than seven days, it has not yet been able to perform close to criteria after six weeks of postsurgical training. Lowering criteria by decreasing the number of days and/or accuracy rate would have allowed the rats to reach criteria. However, those results would actually be false in the sense that the subjects had not learned the discrimination task to a high degree. Flucuations in accuracy then could be attributed to the lidocaine rather than to a learning deficit. So the stringent requirements of the assigned criteria were necessary for true results. The implantation of the cannulae may have caused brain damage that has impaired its ability to perform correctly.

Trainers noted three factors which seemed to affect the subjects' performances. Auditory stimuli easily distracted the rat during its trial. Trainers were allowed to take certain

holidays off, and missing even one day of training caused a drop in subjects' accuracy rate. It was also noted that after the vivarium staff had cleaned cages or changed water bottles, the rats appeared to be agitated for about an hour.

Further research is needed to determine the causal factor of the rats' inability to learn this task. The importance lies in environmental enrichment having limits to the learning and physiological changes it produces. This would give support to the strength of genetic determination in the development of cognitive abilities. If the task used in this study was that difficult, researchers can use it as a highly sensitive memory test.

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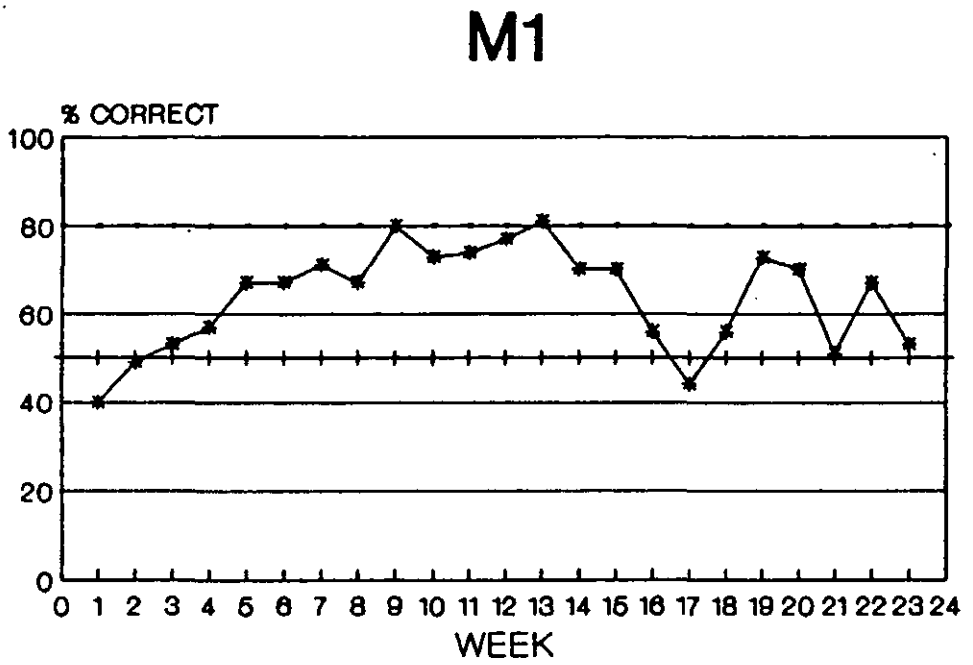
FIGURES

Figures M1-M6 and N1-N6 are graphs showing the average weekly accuracy rates for each rat. Figures M1-M6 represent the six rats on the match-to-sample-task. The nonmatch-to-sample-task rats are on the N1-N6 figures. The 80% and 50% lines are marked for comparison of weekly performance to the levels of criteria and chance. While the average rate for a week is above the criteria level, the average for seven days includes one or more days below 80% which does not satisfy the requirements. The exception is figure M5, week 19, in which the rat reached criteria and figure M5, week 20, in which the rat underwent surgery and recovery.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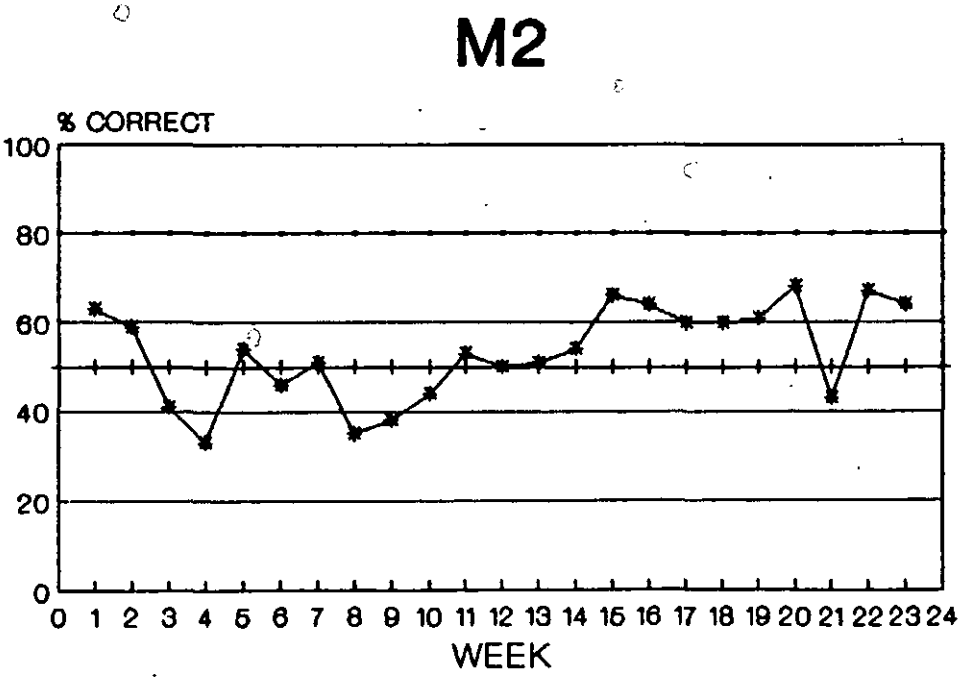
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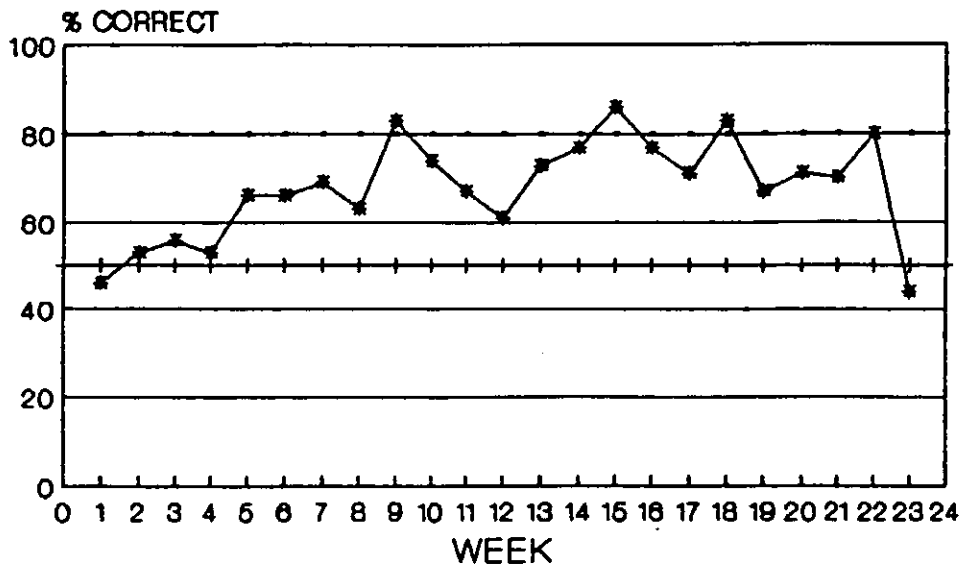
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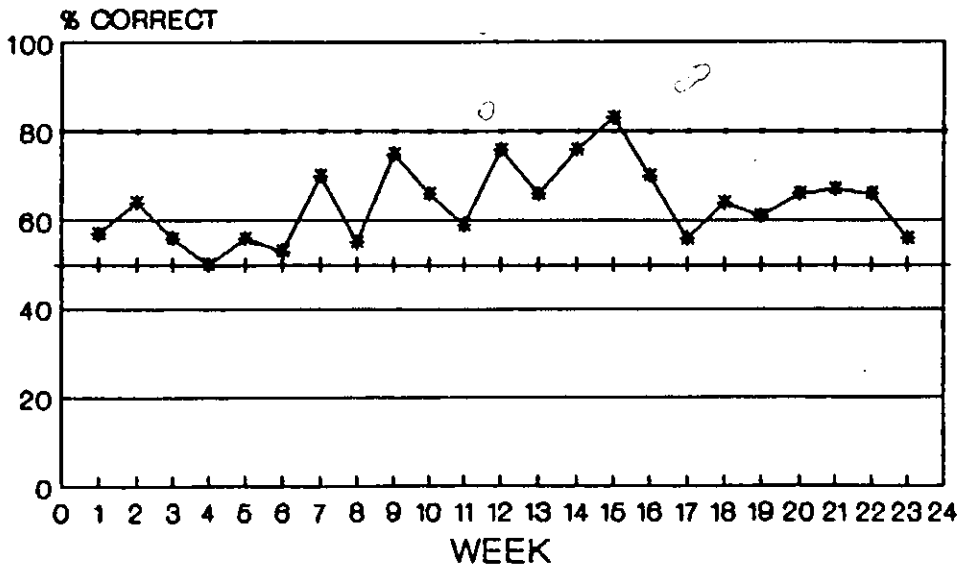
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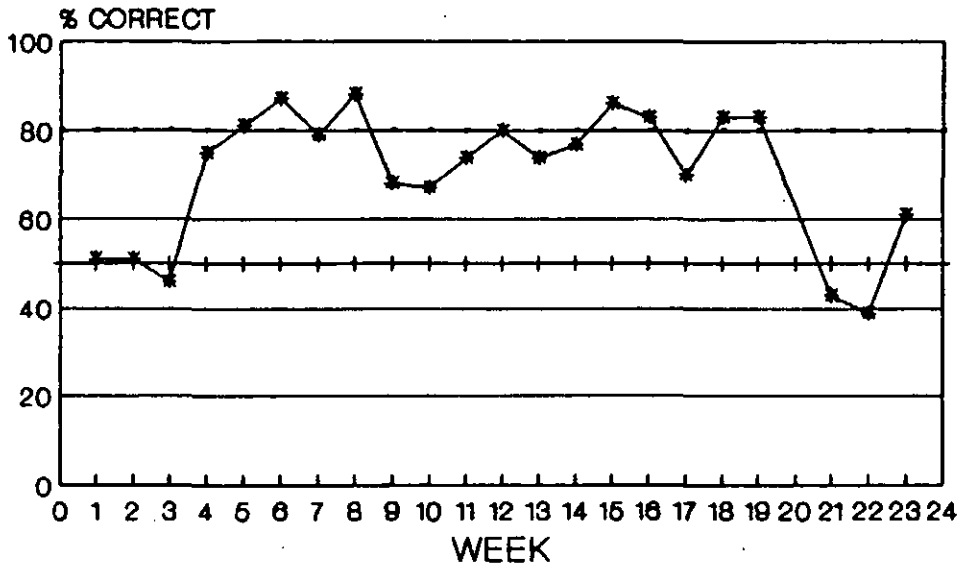
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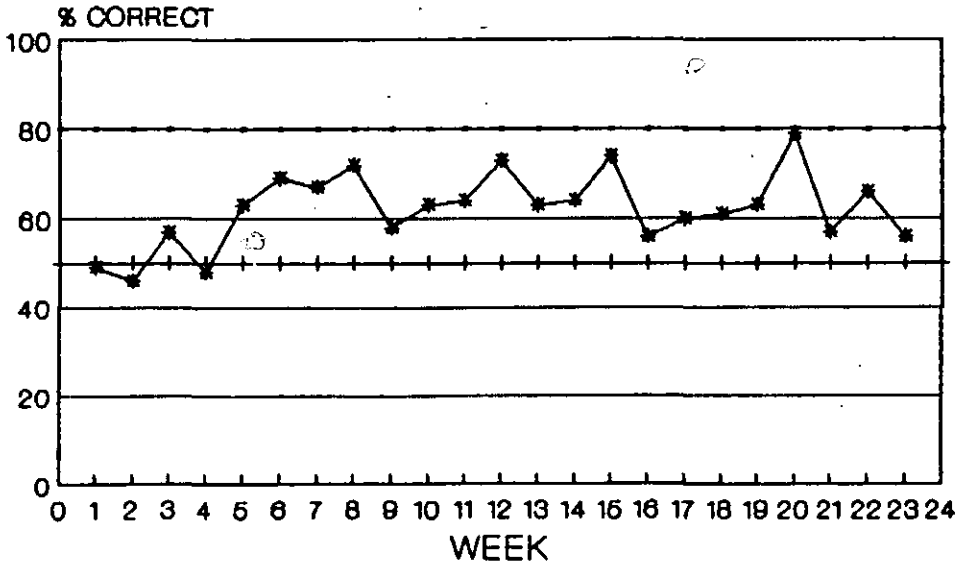
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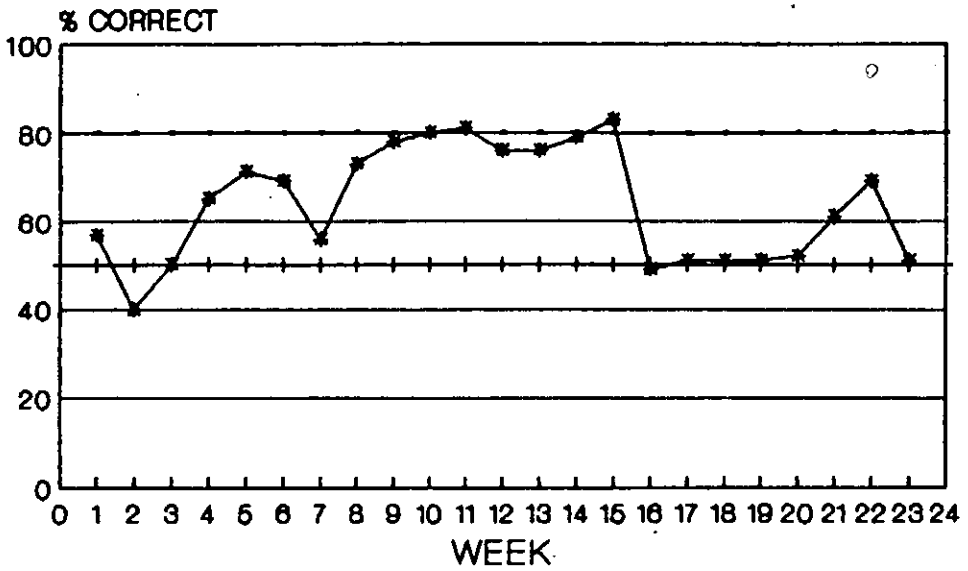
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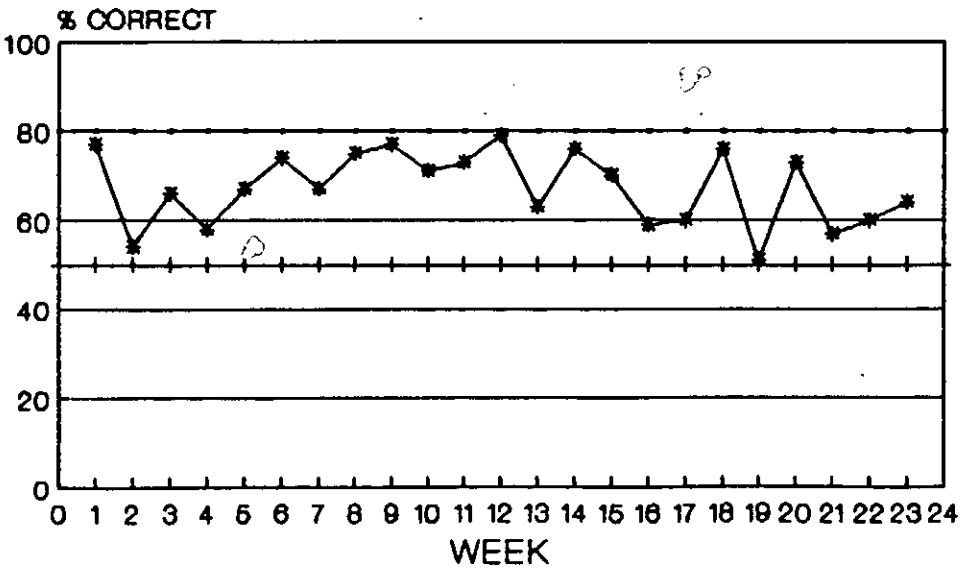
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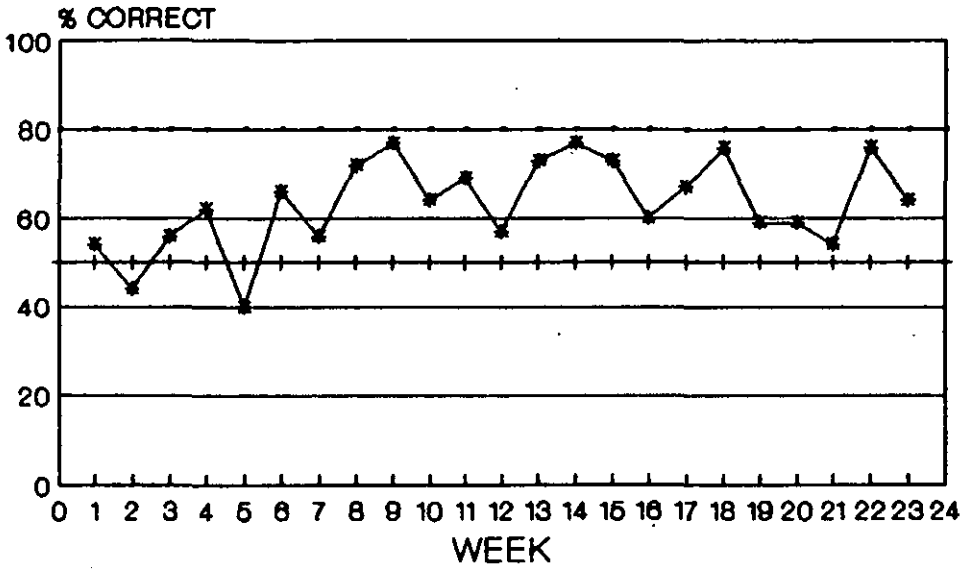
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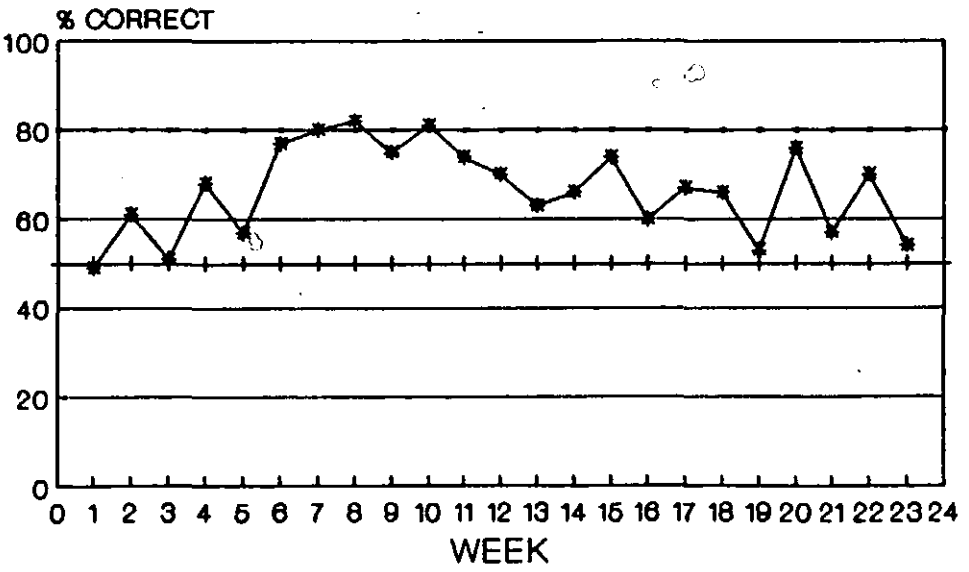
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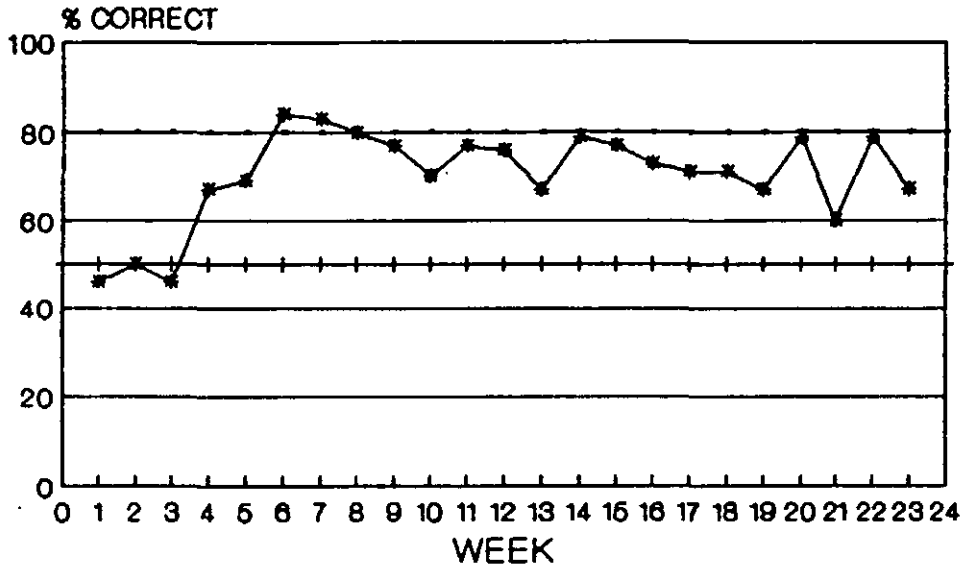
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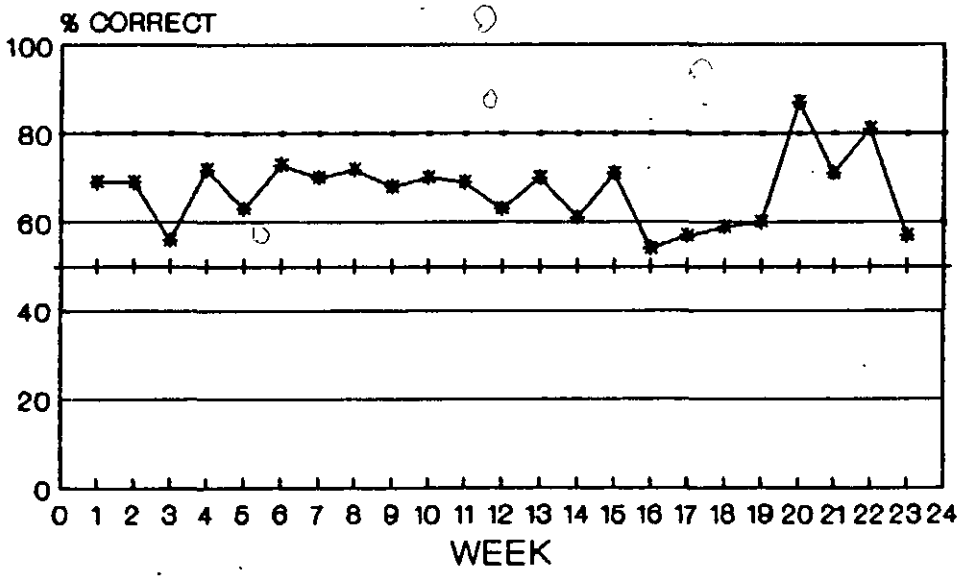
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