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# The effect of amphetamine sulfate upon the behavior and school performance of hyperactive children

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# THE EFFECT OF AMPHETAMINE SULFATE UPON THE BEHAVIOR AND SCHOOL PERFORMANCE OF HYPERACTIVE CHILDREN

by

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# CHAPTER I

## INTRODUCTION

This study was designed to test the effect of amphetamine sulphate on the behavior and academic achievement of children. The chief purpose is to determine whether it achieves a beneficial effect in hyperactive children by reducing the activity level and the degree of impulsiveness while increasing emotional control and lengthening the attention span. As a byproduct to treatment of physical illnesses by drugs, it has often been observed that there are behavioral and psychological changes in the patient. As the study and treatment of human behavior became a focus of interest for medicine and psychology, clinicians have become increasingly interested in deliberately treating deviant behavior pharmacologically. Sakel introduced the use of Insulin in the treatment of schizophrenia about 1930 in Vienna. Metrazol was first used by Meduna in 1935 to treat the affective psychoses, involutional melancholia, and some acute catatonic episodes. It was during this same period, in the 1930's, that reports appeared on the effects of amphetamine sulfate on children manifesting behavior problems of various sorts. The questions for which answers are sought are: Is there a criterion which can be used to predict which children will be beneficially effected by the use of amphetamine sulfate? In what spheres is change observed when amphetamine is administered?

Clinical observation has convinced many psychiatrists and psychologists that amphetamine has a beneficial effect on many children with deviant behavior. Most of the studies are purely observational with no attempt to set up scientific controls. Results are somewhat confusing with some children reported to be functioning at a more satisfactory level, some showing no change with amphetamine sulfate, and some reported to be worse. Primarily, it is reported that with some subjects the medication seemed to serve as a depressant. This is contradictory to previous experience which indicated that amphetamine sulfate served as a stimulant. Previous work has been empirical in nature with no real attempts at adequate controls. The importance of controlled conditions and the testing of definite hypotheses in a manner susceptible to statistical analysis is acute in working with human behavior. This need is strikingly demonstrated by the many assumptions current concerning the use of amphetamine sulfate and the ease with which it is administered in clinical practice. It has been suggested by some that this medication is effective because it gives "a feeling of well-being". Other observers suggest that it is effective with children who have had some particular brain damage in early life or a type of cerebral dysfunctioning.

Despite the fact that much of this still remains in the realm of speculation, amphetamine sulfate is widely used in the treatment of emotionally disturbed children.

The attempt to handle behavior problems easily and quickly has led to increasing use of amphetamine sulfate in an attempt to protect the child in the community, protect his emotional life and control his activity. The ease and economy of administration has led to widespread use. In addition, its effect is immediate, reaching its optimum effectiveness in within twenty or thirty minutes. It has no toxic aftereffects and it wears off within twenty-four hours. This clearly demonstrates why its use is so tempting to the child psychiatrist and the pediatrician. But it has not been clearly indicated that amphetamine sulfate has the definite effect upon the symptomatology mentioned. Each administrator of medication proceeds on his own particular hypothesis. Thus previous material has been difficult to evaluate. The problem presented then is: Can amphetamine sulfate be utilized to improve the behavioral efficiency of some children? If so, what are the criteria for its use? Can amphetamine sulfate be utilized in certain behavior disorders with a degree of predictability as to results?

It is hoped that this research can establish an experimental base for the use or repudiation of amphetamine sulfate in the treatment of certain behavior disorders. The endeavor is to discover the criteria for its use. The experimental procedure is constructed to detect change in hyperactive children who have been given amphetamine under controlled conditions. Thus one might arrive at a higher

degree of predictability of success than has appeared in the literature to date. We are looking also for the areas in which improvement might be most pronounced. This, of course, can be expected to suggest areas for further study.

Because of the questions that still remain unresolved it has become increasingly important to determine with some degree of specificity, the value of amphetamine sulfate. Otherwise, the possibility will always be present that amphetamine is merely serving as a palliative and is a delusion while causing the physician and the psychologist to neglect treatment of basic causes of human behavior.

# CHAPTER II

## SURVEY OF THE LITERATURE

Throughout the literature discussing the use of amphetamine sulfate with adults, the stimulating effect of the drug is mentioned. It is considered to have outstanding anti-depressant features, and its use is indicated when treatment in this direction is the objective. Goodman and Gilman, in their classic work (30), discuss this use of the drug at some length. They refer to it as a stimulant and anti-depressant and report excellent results with its use for narcolepsy, in depressions and in states of exhaustion. They report good results when it is used for psychogenic disorders where depression and fatigue are the outstanding characteristics. It can be easily used by the physician because of its wide margin of safety. That is, there may be a great variation in the dosages without any ill effects. No permanent organic changes have been observed as a result of taking amphetamine sulfate. The medication takes effect within thirty minutes to one hour.

### A. PRELIMINARY RESEARCH WITH ADULTS

Amphetamine sulfate was described in 1910 by Barger and Dale (20) as a group of drugs to which they gave the name "sympatho-mimetic". In 1930 this drug was used in pharmacological studies conducted on animals by Alles, Hartung, Munch, Tainter and Prinzmetal (16). At first their

attention was on the peripheral effects of the drug, but a marked action on the higher nervous centers was also noted. Some observers noted that overdosage, particularly late in the day, led to insomnia. A pressor action was noted by Delray and Pichot (21). This same effect on humans was noted by Kleinmeir and Katz (38). Nathanson (49) reported a definite stimulating action in the central nervous syatem of normal individuals and found the drug reacted favorably in states of persistent exhaustion and fatiguability.

Davidoff and Reifenstein (20) attempted to test the stimulating effect of amphetamine sulfate in 1936, and drew the following conclusions: when amphetamine sulfate was used, the normal group was found to have the largest number of responses in all spheres. The organic group was next and surpassed all the other abnormal groups. Elevation of mood was the least marked response. Of the abnormal cases, 25.5% showed this response while 70% of the normal cases responded thusly. Overtalkativeness was seen in 60% of the abnormal cases, except in the dementia praecox cases where the figure was 28%. In the normal cases the overtalkativeness appeared in 70% of the cases. Hyperactivity was the most frequently observed reaction to amphetamine sulfate, appearing in all of the normal group and 80% of the organic cases. With dementia praecox and psychoneurosis there was considerably less effect. In some cases a decreased motor activity was noted.

In a consideration of general efficiency, it was found again that the normal and organic group showed the most consistent gain. All the normal cases and 80% of the organics showed increased general efficiency. The lack of response in this respect of the psychoneurotics presents a striking contrast.

In general, then, the most marked response in all phases studied was found in the normal group. This was closely paralleled in the organic category. This particular article was discussed in some detail because it in essence summarized all the existing literature prior to 1937. It also submitted the concepts and hypotheses formulated to that time to some sort of experimental design, despite its obvious limitations and subjectivity. Davidoff (18) also completed two additional research projects on the use of amphetamine sulfate. One dealt with the use of amphetamine sulfate with self-absorbed patients, and the other was an eighteen month study of the effects of amphetamine on all types of individuals (19). These two experiments confirmed the impressions of the earlier research outlined above.

Henderson and Gillespie (32), in their standard work, consider amphetamine sulfate to be particularly effective in working with chronic post-encephalitic syndromes. They speak of the symptoms of this syndrome to include the following types of behavior disorders: restlessness, aggressiveness, impulsiveness, erratic but active attention,

irritability and violence. While the medication caused an improvement in this symptomatology, there frequently appears a secondary intellectual deficiency due to a lack of attention. The results are not permanent, however, and disappear with the withholding of medication.

Molitch and Eccles (42) found that when amphetamine sulfate was administered to adults in a normal group it proved invigorating and seemed to have a stimulating action. They also quote People and Guttman as having substantiated this observation. Sargent and Blackman (52) used amphetamine sulfate with forty-eight adults in a mental hospital and gave intelligence tests before and after the administration. The results showed an eight per cent total improvement in test scores with amphetamine. No controls were used, however, and when Molitch and Eccles (47) repeated part of this experiment using placebos also, they discovered that there was also improvement on test scores when only the placebo was used. Myerson and Nathanson (49) later corroborated this as well as the stimulating effect of the amphetamine.

Alles and Feigen (1) conducted a research project with the use of amphetamine sulfate on industrial workers. They showed that the use of the drug appreciably reduced fatigue and increased efficiency in industrial workers. They raised serious questions, however, as to whether this was a continuous or merely a temporary effect. The study tended to demonstrate that its continued use led to a decrease and disappearance of its early stimulating effects.

The early enthusiastic hopes for amphetamine sulfate with normal, psychoneurotic and psychotic individuals had to a great degree collapsed. It had been well established that with adults amphetamine sulfate served as a stimulant. It showed its greatest effect on normal subjects. Those suffering from illness organic in its origin showed the next highest number of responses and exceeded all other abnormal groups. Change of mood seemed to be the least notable response. Most frequently remarked changes were increases in hyperactivity, overtalkativeness, general efficiency. Psychogenic illnesses showed the least response, but amphetamine sulfate might accelerate improvement in patients where recovery was inevitable. It had also been indicated that with organic illnesses, restlessness, impulsiveness, violence, aggressiveness, impaired attention span, and irritability were particularly responsive to amphetamine. Intelligence scores were suggested to be elevated with the use of this medication. Other studies indicated that industrial production could be increased and fatigue reduced. All writers felt, however, that results were temporary and improvement dissipated with continued use or when medication was removed. No change in the illness or in the structure of the personality were found, nor did benefits persist when the drug was removed from the individual. Results of medication

are almost immediate and effects disappear within twenty-four hours of drug removal.

B. AMPHETAMINE SULFATE WITH CHILDREN

While amphetamine sulfate was used with some degree of frequency for children showing deviant behavior during the 1930's, it was on a hit and miss basis, trial and error, with no clear concept as to when its use was indicated. It had no experimental background and no method of measuring and evaluating its efficacy had been attempted.

In 1937 Bradley (10) attempted to organize his experiences with this medication and presented the first paper on the use of amphetamine sulfate with children. The greatest change was noted in school performance. Speed of comprehension and accuracy of performance increased in most cases. It appeared the first day amphetamine was given and disappeared the first day the medication was discontinued. Half of the children, however, did not show this striking change. Emotionally, half of the children became subdued in their responses, and this was considered clinically a social improvement. In many it was accompanied by a feeling of well-being. More irritable, aggressive, noisy, domineering children were reported to become more placid.

Seven children gave only evidence of a feeling of well-being. All showed a widening interest in things around them and a diminishing tendency to be preoccupied. Five became tearful and appeared worried. Only one was reported to have shown effects in the opposite direction, i.e. more

hyperactive, aggressive and irritable. Some change in motor activity was noted in the form of a slowing up with only three becoming more hyperactive. This was startling at the time since it was in direct opposition from what would have been expected as a result of work with adults. However, there was no standardization of observation and only the comments of school teachers and nurses as to performance.

Behavioral effects were seen thirty to forty-five minutes after oral ingestion of the drug. Changes in behavior were at their height during the second and third hour and gradually disappeared over a period of six to twelve hours. In all cases the full effect of the medication was noted on the first day of administration. It continued as long as amphetamine sulfate was taken and left permanently as soon as the drug was discontinued.

In this first experimental attempt to evaluate the use of amphetamine sulfate with children, Bradley (8) commented upon the results:

> "No entirely plausible reason for this acceleration of school performance is evident aside from the fact that a stimulating drug was used. However, at least half of the whole group of children did not show this striking response in school, in spite of the fact that most of them responded in other ways to medication. Only half of them showed favorable mood changes and also shared to a notable degree in the school performance.
>
> "As far as improvement in individual school subjects was concerned the teachers were most impressed by changes in arithmetic, since speed of comprehension and degree of accuracy and quantity of output were all favorably affected.

> "It appears paradoxical that a drug known to be a stimulant should produce subdued behavior in half of the children. It should be borne in mind, however, that portions of the higher levels of the central nervous system have inhibition as their function, and that stimulation of these portions might indeed produce the clinical picture of reduced activity through increased voluntary control. Presumptive evidence that this may be the case is suggested by electroencephalographic studies...Definite abnormalities of the brain rhythms were noted in eleven of these children, eight of whose records showed... 'seizure waves' seen in patients with petit mal epilepsy. All but one of these children with 'seizure waves' became distinctly subdued under the influence... it has been suggested that their appearance indicates impaired cortical functions.
>
> "...From preliminary observation of the thirty children in this series there seems to be very little apparent relationship between a child's response to amphetamine and the conventional clinical characteristics of age, sex, past history, physical condition, reaction type, intelligence and special mental abilities or disabilities." (8, pp. 582-583)

The following year, 1938, Jasper, Solomon and Bradley (36) attempted to evaluate more thoroughly Bradley's suggestion that many children suffering from behavior problems had impaired cortical functioning. They studied 71 children with a variety of behavior problems and found that seventy-one per cent had abnormal electroencephalograms. The abnormalities were marked in fifty-nine per cent. They then concluded that many of these behavior problems considered of a functional nature, in truth had an organic component.

At about this time, Molitch and Eccles (47) ex-

perimented in a more thorough manner with the use of amphetamine sulfate on ninety-three boys between the ages of eleven and seventeen. They tested these boys on placebos and on amphetamine sulfate, as well as with no pill at all.

Several important factors are pointed out in this study that had been overlooked in the earlier ones. One of these is that the individuals tend to show improved performances with a placebo, that is the administration of a pill has a psychological effect reflected in improved performance even though the pill itself has no pharmacological effect. Subjects improved with either the placebo or amphetamine, but they did show greater improvement with the amphetamine sulfate. This was something Bradley did not consider in his research. The age differential also makes these two studies difficult to compare. A further flaw in this study, which the authors themselves recognized, was that test and retest for the intelligence scores was not done on comparable forms of the same test. Rather, two entirely different tests were given. Thus part of the improvement may reflect differences in the tests administered. Because of this it is difficult to judge the significance of the results obtained. The implication is strong however, that amphetamine sulfate did lead to improved performance in these children in the areas tested.

In 1939 Bradley (7) published his empirical findings on twelve years of experience with amphetamine sulfate.

"Specific behavior responses...(to ampheta-

> mine sulfate)... 50 to 60% of the children becoming more subdued, 15 to 25% showing no change, 20% showing increased activity and 5% showing an acceleration of school progress only. Clinically these reactions indicated 60 to 75% symptomatic improvement, 15 to 25% no change and 10 to 15% unfavorable responses. Children with a variety of clinical diagnoses were benefited with no evidence of tolerance or addiction following prolonged administration.
>
> "...The conclusion is drawn that these drugs influence children's behavior by altering their emotional reactions to distressing situations. It offers the practitioner readily available and easily controlled pharmacologic approaches to the symptomatic treatment of children's behavior disorders." (7, pp. 35-36)

Bradley also attempted to explore the possibility that improvement with amphetamine sulfate might somehow be correlated with diagnosis. For this purpose he divided the children into four categories: behavior disorders of psychogenic origin, behavior problems associated with convulsive disorders, psychopathic personality, children with schizoid personality. There seemed to be little significant difference between groups in the response to amphetamine sulfate except for the schizoid personality group which showed the least improvement. It was pointed out that hyperactivity was frequently associated with behavior problems in children and that amphetamine sulfate seemed to have its greatest effect on the activity level. At this point in research it was felt that the effect was chiefly obtained from the feeling of well-being which pervaded the children when amphetamine sulfate was administered.

C. CONCEPT OF USE FOR ORGANIC DYSFUNCTION IN CHILDREN

The idea that there might be a cortical impairment in a preponderance of children who showed behavior disorders had been abandoned after a study was made by Cutts and Jasper (17). They studied the effects of amphetamine sulfate on behavior problem children who also had abnormal electroencephalograms. About one half of the patients were distinguished by marked improvement in behavior with amphetamine therapy. Changes in the electroencephalogram, however, did not correlate with clinical changes produced by the drug.

Lindsley and Henry later repeated this research in more detail (44). They found that behavior improved markedly with the administration of amphetamine sulfate. While a number of statistically significant changes occurred in the electroencephalograms they were not marked changes and were not in proportion to the changes in behavior noted. Also the electroencephalogram changes were not always consistent from subject to subject or from one head area to another. They therefore concluded that changes in behavior produced by amphetamine sulfate were independent of changes in the electro-cortical abnormalities.

McNamara and Miller (48) working with college students found no increase in efficiency in solving standard multiplication problems when amphetamine sulfate was used, but the subjects reported feeling mentally stimulated when the drug was first administered. Barmack (4) also worked with college students and concluded that amphetamine sulfate im-

proved the "inclination rather than the ability of the students to perform the tasks at hand". This led Bradley and Green (14) to examine the psychometric performance of children receiving amphetamine sulfate. In general there was no striking change in the intelligence quotient when amphetamine sulfate was administered. Attempts to correlate change with age, sex, personality type or clinical problem gave no noteworthy results. More startling was the fact that in those children where school performance improved markedly there were no better results in psychometric performance with medication than with those children who had not shown this improvement in school performance. Results on psychomotor tests were equally inconclusive.

Bradley and Bowen (13) shortly later published another article in which they found that amphetamine sulfate subdued the activity of fifty-four of one hundred children on whom it was used. They warned at this point that the medication should only be considered a supplementary aid in child psychiatry and was not a substitute for the more basic psychotherapy or environmental improvements.

Bender and Cottington (6) attempted a research project with amphetamine sulfate and children diagnosed as psychoneurotic, neurotic behavior disorders, psychopathic personality, organic brain disease, and schizophrenia. They, too, gained the impression that amphetamine sulfate was a useful adjunct to treatment of the neurotic child. They

felt that it gave him a feeling of well-being and temporarily allowed him to feel secure and loved.

> "In this frame of mind he can face his difficulties, express his aggressive impulses without overwhelming fear of consequences, and obtain relief from inner tension and anxiety. The art productions and other means of expressing the fantasy life of these children reflect these processes as they take place.
>
> "In the more severely neurotic child ...(amphetamine sulfate) acts only as an expedient to help the child adjust in an environment where he can later find help for his deeper conflicts, and leads to an evasion of those problems during the period of administration. Here, too, the art and fantasy production show an inhibition which parallels the evasion noted in the personal therapeutic approach during medication.
>
> "Fear, depression and sexual tension in the child are often completely relieved ...as is hyperkinesis appearing on a neurotic basis. Activity is frequently integrated and made more productive, and the relationship to the group is thus facilitated.
>
> "...has no appreciable effect upon the behavior of children with developmental brain defects or with schizophrenia and its effect upon the psychopathic personality was in all respects unfavorable. Consequently its use in a controlled ward setup may be an aid in the differential diagnosis of some obscure problems..."(6, p.80)

Korey (39) did a study upon the effects of amphetamine sulfate on psychopathic and neurotic juvenile delinquents between the ages of fourteen and nineteen. The writer pointed out that his results were in contradiction to Bender and Cottington since they reported no favorable results when amphetamine sulfate was used with psychopaths.

Korey felt that the psychopaths reacted as well to the drug as did the neurotic delinquents. The author could offer no answer to why one child should respond to this medication and not another. He too felt that no degree of predictability had been arrived at. All changes were considered superficial and disappeared as soon as medication was withdrawn.

Bakwin (4) in reviewing some of the research in 1948 could still point only to conclusions reached by Bender and Bradley that amphetamine sulfate depended for its efficacy on its ability to produce a feeling of well-being in children and thus enable the child to face more readily the tasks before him.

In 1948 Rosenfeld and Bradley (51) presented their concept of an organic syndrome in children. Much of this concept flowed from Bradley's earlier work with the use of amphetamine sulfate which has been described in some detail in the preceding section of this chapter. These writers outline this organic syndrome of behavior in children as consisting of the following symptoms:

1. These children are hyperactive. The activity is involuntary in nature and is almost constant. This hyperactivity may appear from infancy to about six years of age. Its earliest form may be in precocious development, early sitting, standing, walking, etc. They cannot sit still, are restless and fidgity.

2. They have short attention spans and limited

powers of concentration. Whether in school or at play the children cannot stay at one task or game for long and tend to change interests very rapidly. They seldom complete a task that they have undertaken.

3. They are variable in mood, performance and behavior. They are unpredictable and even school grades may be variable.

4. The children are impulsive and act without considering the consequences. They cannot brook interference and act on every desire with apparently no tolerance for delay of gratification.

5. They are usually irritable children. They may have little frustration tolerance, and interference with their activities, or asking for obedience, will bring on an angry tantrum.

6. They are explosive children. Their responses are intense and when they have a tantrum they may seem completely out of contact in their demonstrations.

7. Finally, these children perform poorly in school. This would be expected from the items listed above. There may also be a specific learning difficulty, most particularly in arithmetic. These problems seem to be related to the visual-motor area.

Meanwhile in France, Gastaut (27) published a paper on a method of studying activities of the brain in 1950 by the photo-metrazol technique. This was further amplified

in another paper with Hunter (28). In essence these publications seemed to demonstrate that types of abnormal behavior might arise from damage to, or interference with the functioning of the diencephalon. Thus was suggested a new area, in the lower brain center rather than in the cortex, where brain damage might create deviant childhood behavior.

In the same year, Delay, Pichot and Deniker (21) reported on their use of amphetamine sulfate with manic depressive patients in manic excitement. They found that, contrary to expectations, amphetamine frequently had a quieting effect, as though it were a sedative rather than a stimulant. They felt the effects confirmed their premise that amphetamine sulfate acts upon the diencephalon.

Denhoff, Smirnoff and Holden (23) discussed the possible etiology of such brain damage and the consequent syndrome which appears. The factors are roughly similar to those which cause cerebral palsy. Any injury prenatally, during birth or in the first five years of life may result in this organic cerebral dysfunction and the consequent symptomatology if there is damage to the diencephalon. Prenatally it may be due to maldevelopment, attempted abortion or an interference with fetal blood supply or oxygen supply. An infection of the mother, such as German measles and the like may also result in diencephalon injury.

During childbirth innumerable accidents attending

delivery may result in such diencephalon damage. These are also given new significance by Arey and Dent (3) and by Greenacre (31). Even in the normal delivery without untoward incident there is believed to be an amount of internal cerebral hemorrhaging which could cause diencephalon damage. Arey and Dent (3) indicate that there is a tendency for hemorrhages to occur at the end loops joining the arterial and venous systems in the brain. Postmortem studies have shown that such hemorrhages do take place around the terminal vein of the thalamus.

There are also post-natal causative factors for the presence of this organic syndrome. These may be due to infection, to injury, to anoxia, to hemorrhages and to central system disorders. Laufer, Denhoff and Rubin (41) outline some of these elements. Bradley (11) had previously indicated that the behavior problem with which we are concerned was often seen in epileptic children, suggesting that it accompanied damage to the central nervous system. Denhoff and Holden (23) found that twenty-three per cent of their cerebral palsy cases also had the organic syndrome.

Some researchers have found disease of the diencephalon may lead to behavior similar to that found in the organic syndrome. Timme (25) and Hill (33) both feel after investigation that there occurs a decrease or disappearance of much of the inhibition which the higher brain centers customarily impose on the lower brain centers. This may be due to a prefrontal lesion, an interruption of certain tracts between

the neocephalic and paleocephalic levels or the destruction or disintegration of some integrating structure. Jasper (35) did some experimental work to show that there are corticofugal projections reaching from the cortical areas which exert an effect on the thalamic and mesencephalic reticular formations. Thus it appears that the neocortex does have a modifying effect upon diencephalic functions.

Laufer, Denhoff and Rubin (42) attempted to test the hypotheses concerning the presence of a lesion in the diencephalon which causes the organic syndrome of behavior by use of Gastaut's photo-metrazol technique. They further postulated that the syndrome disappears with increased maturation and that until this occurs, amphetamine sulfate controls the behavior at the diencephalic level. In other words, this research dealt with the measured physiological effects of amphetamine sulfate. This research had been further stimulated and given direction by the statement of Marazzi (34) that the effect of amphetamine sulfate on the central nervous system "produces a true primary inhibition at all sympathetic synapses just as it does at many sympathetic neuroeffector junctions". Hodge and Hutchings (33) also felt that they had shown that amphetamine sulfate had a depressant effect at the synapses. Thus they reasoned that children suffering from organic cerebral dysfunction had a condition where impulses crossed the synaptic connection too swiftly and without sufficient resistance to

such impulses in the synapses, and amphetamine sulfate offers the necessary resistance.

The photo-metrazol test revealed that there was an abnormally low metrazol threshold in those children suffering from organic cerebral dysfunction, and this threshold was elevated by the administration of amphetamine sulfate. Thus it was demonstrated that amphetamine sulfate has a specific effect. It had been previously shown by Gastaut and Hunter (28) that intravenous metrazol acted selectively at the thalamic system. Laufer further adds:

> "The considerations just presented have suggested that metrazol acts by lowering the level of synaptic resistance to transmission within the central nervous system and particularly at the level of the thalamus.
>
> "This would suggest that amphetamine, which we have shown capable of raising the photo-metrazol threshold, does so by raising the level of synaptic resistance in the diencephalon, thus restoring normal relationships." (42, p. 5)

After several years of observation of the use of amphetamine sulfate with children there appeared a general concurrence among the various writers as to the areas of behavior affected by this drug. These areas were activity level, impulsiveness, attention span and emotional control. These observations had not been submitted to rigid experimental conditions and statistical analysis. The question of a diagnostic criterion to determine which children would react in a predicted manner when given amphetamine sulfate had also come under consideration.

The suggestion that amphetamine acted as a depressant at the synaptic connections in the diencephalon led to the inference that only children suffering from organic cerebral dysfunction reacted in the predicted manner when this drug was administered.

An experiment was conducted by the present writer to examine the proposition that amphetamine sulfate was effective only with children suffering from some type of organic brain damage. Experts at diagnosing this condition selected an experimental group of children with this condition and a control group of normals. The hypothesis that "children with organic cerebral dysfunction will demonstrate improved performance after the administration of amphetamine sulfate," was tested by means of the Stanford-Binet, the Seguin Form Board, the Porteus Mazes and the Bender-Gestalt Visual Motor Test, as well as by the use of a behavioral rating scale designed to detect change in hyperactivity, impulsiveness, irritability and length of attention span. Testing and observations were made both on a placebo and on medication.

The results obtained from this study proved to be inconclusive and could not be used to substantiate the hypothesis. With both the testing situations and the behavioral rating scale, the statistical difference observed did not reach the necessary level of confidence. The best that could be inferred was that whatever results were ob-

served were not brought about by the interaction of medication and subjects with organic cerebral dysfunction. There was an observation of marked changes in some subjects, but this might be in either the experimental or control groups. The research left the examiner still with the problem of determining a criterion for prediction of which children would react in a specific manner to amphetamine.

A review of the results gave rise to the empirical hypothesis that hyperactivity was the factor common in those subjects who showed the predicted results when amphetamine sulfate was administered. A group was constructed of those subjects who had been rated hyperactive on the behavioral rating scale when on the placebo. Ten such subjects come from the experimental group and seven from the control group. This group was then compared with itself for results on the behavioral rating scale while on amphetamine sulfate and on the placebo. On amphetamine sulfate hyperactivity diminished in fourteen, impulsiveness diminished in eleven, and attention span lengthened in fourteen.

On the basis of the results obtained with this latter grouping together with the observations made during the initial experimentation, it was determined to construct new hypotheses and a new experimental design to test the general proposition that amphetamine sulfate in hyperactive children produces more efficient behavior.

# CHAPTER III

# HYPOTHESES AND EXPERIMENTAL DESIGN

## A. Hypotheses

The literature culminating in the investigation of the use of amphetamine sulfate with children suffering from organic cerebral dysfunction suggested the general hypothesis: Hyperactive children will demonstrate more efficient behavior when administered amphetamine sulfate. Children considered hyperactive are those who consistently demonstrate a level of activity in excess of the "normal" child. More efficient behavior is demonstrated in this investigation by a decrease in gross activity, a decrease in impulsiveness, greater emotional control, a longer attention span and improved scholastic performance. The following experimental hypotheses are utilized to test the general hypothesis:

1. Hyperactive children will demonstrate less gross activity, as measured by a behavioral rating scale, when administered amphetamine sulfate.

2. Hyperactive children will demonstrate less impulsive behavior, as measured by a behavioral rating scale, when administered amphetamine sulfate.

3. Hyperactive children will demonstrate a greater degree of emotional control, as measured by a behavioral rating scale, when administered amphetamine sulfate.

4. Hyperactive children will demonstrate a longer attention span, as measured by a behavioral rating scale,

when administered amphetamine sulfate.

5. Hyperactive children will demonstrate improved scholastic performance, as measured by a standard test of school achievement, when administered amphetamine sulfate.

## B. Experimental Design

The basic design of the experiment called for selection of hyperactive and non-hyperactive children and testing them for effects of amphetamine sulfate. To control for the pharmacological effects of the drug rather than the psychological effects of its administration, the subjects, in balanced order, were given amphetamine sulfate and a placebo on different days and tested under each condition. Reactions under the placebo thus provide a comparative baseline for judging the reactions to the drug. The independent variables are the presence or absence of hyperactivity and the ingestion of amphetamine sulfate as compared to a placebo. The dependent variables are rating scale scores and actual test performance used to measure the differences between groups and between pharmacological conditions.

### Independent Variables

All subjects were drawn from a residential treatment center for disturbed children. The clinical psychologist, the head nurse and the group leaders in charge of the children were asked to divide all the children into two groups, those who were hyperactive and those who were not. Only those children were used as subjects about whom all the evaluators

agreed. Twenty were placed in each group, the hyperactive group known as Group A and the non-hyperactive group known as Group B for purposes of this study. The names of all subjects with the designation of whether they belonged in Group A or Group B were given the Chief Clinical Psychologist by those making the selection of hyperactive and non-hyperactive children. He discarded those on which there was not unanimous agreement and used the remainder to form the control and experimental groups. Except the clinical psychologist, no one, including the writer, knew into what category any subject fell.

The psychologist then placed two 5 milligram tablets of amphetamine sulfate in each of two pillboxes for each subject. The same was done with the placebos. The pills are pink and heart-shaped with the placebo identical with the medication in size, shape and color. On each box was placed the subject's name and a code number which would later identify the pill for a particular day as amphetamine sulfate or placebo. The clinical psychologist then made out a list for an order in which the subjects would be observed so that half of each group would receive the medication first and half the placebo first. For the second period of observation two weeks later the order was reversed.

Two days preceding the period of observation, the nurse on duty was given the pill boxes for the subject. The pills were given by the nurse who regularly administered all medi-

cations between 7:15 and 7:30 A. M. This was given the day before the period of observation as well as the day of observation. This was done at the same time and in the same manner that all other children receiving medication were having it administered. No comment of any kind was made to the child and the subjects apparently accepted this as part of regular routine. All pill boxes were returned to the examiner as a further check.

At 9:00 A. M. the subjects went to their regular classrooms according to their usual schedule. Since the medication attains its optimum effect within twenty to thirty minutes and does not wear off from twelve to twenty-four hours, the testing and observation were done well within the period when maximum effects of the medication could be expected.

Controlled Variables

Several variables could be controlled which might conceivably effect the results. These were the setting within which the investigation took place, the subjects' familiarity with the environment, the order of testing and observation, the time of observation and the observers.

All subjects were patients at a small neuro-psychiatric hospital. Only those who had been resident for three or more months and were not schizophrenic nor convulsive were used. The age range at the hospital is six to twelve. Children tend to stay for a considerable period of time so

that the population remains fairly stable. During the period of this study there were no admissions nor discharges. From the time of admission all of the child's activities take place within the buildings or grounds of the treatment center. This includes schooling. The children are divided into groups for living arrangements and management according to age and capability. Each group is cared for by guides, all college graduates, who serve in the capacity of house parents.

Between 10:30 A. M. and 11:45 A. M. the subjects were given a free play situation in which they could do whatever they pleased within the play area. This was not a unique situation in their daily living. During this period, each subject who was being observed for that particular day was rated for four traits according to the appropriate Fels Child Behavior Scales by three observers.

The same observers rated the same child each time. The observers were the guides who customarily care for the children. These guides are all college graduates who are from time to time called on to make observations of the children for research and clinical purposes. Prior to the first day of observation, the purpose of the research was explained and copies of the rating scale shown. Instructions were given as outlined for the rating scales (50). All rating scales were handed to the examiner immediately after the period of examination.

Two variables which might have an effect on the results were equated. These were age and intelligence.

Table I demonstrates the age distribution for Group A and Group B. The range for Group A is from seven to eleven, and for Group B the range is eight to twelve. The mean for Group A is 9.5 years as contrasted with a mean of 9.8 years for Group B. The median age for both groups is 10.

Since one of the admission requirements of the center is that a child be of average intelligence or higher, the composition of both groups is of subjects with intelligence quotient of 90 or higher as determined by the Wechsler Intelligence Scale for Children. The distribution of intelligence quotients for both Group A and Group B is given in Table II. The range of I. Q.'s for Group A is from 90 to 130, and for Group B the range is from 90 to 129. The mean for Group A is 106 and for Group B it is 105. These non-significant differences show both groups are drawn from the same population with respect to age and intelligence.

Dependent Variables

Two instruments were used to measure the dependent variables in this research. The first is the ratings on the behavioral rating scale and the second is the scores on the scholastic achievement test.

For rating scales the Fels Child Behavior Scales (50) were used. These had been independently evaluated for re-

TABLE I

AGE DISTRIBUTION OF GROUP A AND GROUP B

| Age | Group A | Group B |
|---|---|---|
| 7 | 1 | 0 |
| 8 | 3 | 3 |
| 9 | 5 | 5 |
| 10 | 7 | 6 |
| 11 | 4 | 5 |
| 12 | 0 | 1 |
| N | 20 | 20 |
| Mean Age | 9.5 | 9.8 |
| Median Age | 10 | 10 |

TABLE II.

DISTRIBUTION OF INTELLIGENCE QUOTIENTS OF GROUP A AND GROUP B

| I. Q. | Group A | Group B |
|---|---|---|
| 90-99 | 7 | 7 |
| 100-109 | 8 | 8 |
| 110-119 | 2 | 3 |
| 120-129 | 2 | 2 |
| 130 and over | 1 | 0 |
| N | 20 | 20 |
| Mean I. Q. | 106 | 105 |

liability and validity. There are thirty of these scales, each for a separate behavioral symptom and each individually validated. Four were used for this study, for frequency of gross activity, emotional control, impulsiveness and attention span. Each scale consists of a short explanation of the factor being measured at the top of the sheet. On the left hand side of page running vertically is a ten centimeter line. On this line are certain measured intervals. On the right hand side opposite these measurements are clues describing kinds of observed behavior. The observer is to make a mark on the vertical line at a point which most closely corresponds to the subject's behavior during the period of observation. Scoring is then accomplished by measuring with a centimeter ruler. According to instructions given with the scales only changes of 15 centimeters or more are significant in indicating a true change.

Appendix A illustrates the rating scale used to measure the frequency of gross activity. Evidence for reliability is given by the Fels Institute in terms of correlation between individual raters and correlations with other measures or communality of the single scale with the remaining scales. Reliability figures established for the scale of frequency of gross activity are .90 for the inter-rater coefficient and .89 with an external variable. In a three factor communality the reliability coefficient was .88.

While the constructors of these scales feel that in a sense they are self validating by definition, since they

measure the description of the traits given in the clues, they offer further evidence for validity in correlating the scales with other measures and with each other, since each scale is an independent measure. Frequency of gross activity had a coefficient correlation of .89 with "vigor of activity" and -.72 with "physical apprehensiveness". Thus the high correlation anticipated between "frequency" and "vigor" of activity is found and the minus correlation with "physical apprehensiveness" is also found.

Appendix B shows the rating scale used for estimating the degree of impulsiveness. The inter-rater coefficient of correlation was .91. This was the last of the rating scales devised in this series at the Fels Institute and no correlation was established either with an external variable or in three factor communality. Thus with this trait reliability is in terms of the inter-rater correlation.

In establishing validity for the scale on impulsiveness, the coefficient of correlation with "tenacity" was -.76, with "emotional control" -.46, and with "obedience" -.18. This is as would be anticipated since these traits are to a great extent contrary to what one would expect to find in the impulsive child. On the other hand, we find positive correlations with those traits usually expected to have some resemblance to impulsiveness: ⁄.27 with "emotional excitability" and ⁄.13 with "suggestibility".

The scale for emotional control measurement is found

in Appendix C. The inter-rater coefficient, found to establish reliability, was .89 and the coefficient of correlation with an external variable was .83. In a three factor communality the figure was .83.

When this trait was correlated with other scales for the establishment of validity figures, it was found to have a coefficient of .72 with "conformity" and .52 with "attention span". With "obedience" it was .71. When evaluated against traits which are considered to be of an opposite characteristic, the coefficient was -.81 with the scale for "emotional excitability", -.27 with "aggressiveness" and -.68 with "quarrelsomeness". Thus we find positive correlations with those traits where emotional control would seem to be necessary and minus correlations with those traits which in themselves are evidence of lack of emotional control..

The last of the Fels scales used in this study deals with attention span. This scale is shown in Appendix D. The inter-rater coefficient of correlation is .93, while the coefficient with an external variable is .76. In a three factor communality the coefficient of correlation is .57.

For validity the following figures are offered: Attention span scale has a coefficient figure with "planfulness" of .76 and with "emotional control" of .52. On the other hand, the coefficient is -.37 with "resistance" and -.45

with "emotional excitability".

The traits chosen from the "Fels Child Behavior Scales" for use in this research are reported to have extremely high reliability. The validity has also been shown to be exceptionally good. There is evidence from the figures given to indicate that there is some overlapping of the scales, but this is felt to be inevitable in dealing with human behavior. On the whole the scales do seem to be measuring the trait described in terms of the definition of that trait, its accepted usage and in line with the cues given to measure the traits.

To measure scholastic performance, the California Standard Achievement Test was used. This is a group test of academic achievement widely used throughout the school systems of the United States. It gives a raw score which is translated into a grade placement and a scholastic profile. Since there is only one form of this test, all of the odd numbered problems were given to half of the subjects first and the even numbered problems on the second administration. The other half of the subjects were given the test in the opposite order. Grade placement scores were used, and a change of three months or more in score used as the criterion of more efficient academic performance.

The dependent variable is handled in terms of improved or unimproved from the placebo to the amphetamine sulfate rather than the degree of improvement, since this is our

primary concern. In other words, interest was centered in whether there was significant improvement in behavior and test scores with the administration of medication and not with the amount of improvement. "Improvement" in the sense used in this research refers to more efficient behavior in terms of the experimental hypotheses.

This made the data particularly amenable to handling by non-parametric techniques. The method of choice was the Mann-Whitney test. A level of confidence of .05 was set up as the criterion for acceptance of the hypothesis.

# CHAPTER IV.

## RESULTS

It was the purpose of this study to determine the effect of amphetamine sulfate on hyperactive children as manifested in certain specific areas of behavior and performance. The hypotheses may now be stated in operational terms as follows:

1. The incidence of improvement with amphetamine sulfate as compared with placebo would be significantly greater among hyperactive children as measured by the Fels Behavior Rating Scale for gross activity, and the use of the Mann-Whitney test of significance.

2. The incidence of improvement with amphetamine sulfate as compared with placebo would be significantly greater among hyperactive children as measured by the Fels Behavior Rating Scale for impulsive behavior, and the use of the Mann-Whitney test of significance.

3. The incidence of improvement with amphetamine sulfate as compared with placebo would be significantly greater among hyperactive children as measured by the Fels Behavior Rating Scale for emotional control, and the use of the Mann-Whitney test of significance.

4. The incidence of improvement with amphetamine sulfate as compared with placebo would be significantly greater among hyperactive children as measured by the Fels Behavior Rating Scale for attention span, and the use of the Mann-Whitney test of significance.

5. The incidence of improvement with amphetamine sulfate as compared with placebo would be significantly greater among hyperactive children as measured by the California Achievement Test, and the use of the Mann-Whitney test of significance.

It will be recalled that improvement is defined as a difference of 1.5 centimeters on the Fels Behavior Rating Scale or a difference of three months in grade placement on the California Achievement Test. Before reporting the results it is necessary to consider the reliability of ratings on the scales employed.

### A. INTER-RATER RELIABILITY

The reliability of the raters was calculated separately for both Group A and Group B when the subjects were receiving the placebo and when they were receiving the medication. Correlations were computed between the individual raters for each trait being investigated. Thus rater A was correlated with rater B and then with rater C. Rater B was correlated with rater C. The means of these coefficients of correlation for each trait with and without amphetamine were also compiled.

The results for Group A and Group B are given in Table III. These correlations are quite high compared to those usually elicited with the use of rating scales. This is true not only of the means but of the correlations between individual raters. This kind of consistency compares favorably

TABLE III.

RELIABILITY OF BEHAVIOR RATINGS.
PRODUCT MOMENT CORRELATIONS

N = 20

| RATERS | Frequency of Gross Activity | | Impulsiveness | | Emotional Control | | Attention Span | |
|---|---|---|---|---|---|---|---|---|
| | Plac. | Amph. | Plac. | Amph. | Plac. | Amph. | Plac. | Amph. |
| | | | Group A | | | | | |
| A and B | .87 | .90 | .92 | .72 | .80 | .70 | .85 | .73 |
| A and C | .87 | .97 | .94 | .80 | .86 | .73 | .86 | .87 |
| B and C | .70 | .88 | .89 | .91 | .89 | .74 | .87 | .78 |
| Mean | .81 | .92 | .92 | .81 | .85 | .72 | .86 | .79 |
| | | | Group B | | | | | |
| A and B | .63 | .79 | .80 | .79 | .82 | .93 | .88 | .92 |
| A and C | .63 | .90 | .80 | .68 | .87 | .89 | .82 | .90 |
| B and C | .70 | .90 | .86 | .82 | .88 | .91 | .88 | .90 |
| Mean | .65 | .86 | .82 | .76 | .86 | .91 | .86 | .91 |

with the results obtained at the Fels Institute when reliability figures were secured to establish the reliability of the scales. In most cases the correlations in this study with Group A were higher than those in the Fels study, probably due to the more gross behavioral deviations in this hyperactive group.

## B. FELS CHILD BEHAVIOR SCALES

1. Frequency of Gross Activity. The final compilations obtained with the scale measuring "frequency of gross activity" are shown in Table IV. It should be remembered that it was necessary to have a change of 1.5 centimeters or more as measured on the scale to record change. With these conditions, Group A (the hyperactive group) gave improvement in eighteen cases while two were unimproved, when amphetamine sulfate was administered. On the other hand, in the control group not one subject showed the same kind of change with medication. The mean score for Group A on the placebo was 7.93, and on amphetamine 4.97. The means for Group B were 4.44 on placebo and 5.81 on amphetamine. These figures verify the selection of the subjects for both groups, since the mean for Group A indicates that its gross activity is above the norm as established by the scales while on the placebo, the equivalent of no medication. Group B, however, has a mean which is close to the mid-point in the scale. Further inspection slso shows that the groups move in opposite directions when medication is administered to the subjects.

TABLE IV.

FREQUENCY OF GROSS ACTIVITY WITH AMPHETAMINE SULFATE

| | Improved | Unimproved | Total |
|---|---|---|---|
| Group A | 18 | 2 | 20 |
| Group B | 0 | 20 | 20 |
| Total | 18 | 22 | 40 |

When the Mann-Whitney test was applied to the data by comparing the groups for rank order with respect to change of score with amphetamine and placebo, further support was provided for the hypothesis. With R equalling the sum of the ranks, $R_1$ was 230 and $R_2$ was 590. This gives a value of 4.9 and a $p<.01$. We are thus able to accept the first of the hypotheses: hyperactive children will demonstrate less gross activity, as measured by a behavioral rating scale, when administered amphetamine sulfate

2. Impulsiveness. The data gathered in using the scale to measure impulsiveness also provided figures in the direction of the hypothesis. The mean of Group A on the placebo was 4.63, and the mean on medication was 7.23. Thus the means indicate less impulsive behavior for the group when amphetamine sulfate is given. Group B had a mean of 6.04 with the placebo but 5.98 when the subjects were receiving amphetamine. With this group there is little movement, a slight trend in the opposite direction of Group A. One can say that the two groups are affected differently by the use of the medication.

Table V shows the distribution of improvement in each group when amphetamine was administered. In Group A fourteen improved and six were unimproved. In Group B five improved while a total of fifteen were unimproved. Group A, which had been seen while on the placebo to be composed of impulsive children, with medication was rated with the be-

TABLE V.

IMPULSIVENESS WITH AMPHETAMINE SULFATE

| | Improved | Unimproved | Total |
|---|---|---|---|
| Group A | 14 | 6 | 20 |
| Group B | 5 | 15 | 20 |
| Total | 19 | 21 | 40 |

havioral rating scale as being composed of well controlled, non-impulsive subjects.

With the use of the Mann-Whitney test, $R_1$ equalled 320 and $R_2$ was 450. The z score was -2.46, giving a $p < .03$. According to the criterion established, this allows for acceptance of the second hypothesis: hyperactive children will demonstrate less impulsive behavior, as measured by a behavioral rating scale, when administered amphetamine sulfate.

3. Emotional Control. The rating scale assessing "emotional control" produced a mean for Group A of 4.39 on placebo and 7.2 on medication. Again we see the movement of this group from a low to a high degree of emotional control. Group B, on the other hand, had a mean of 6.55 with the placebo and 5.63 with medication. And the phenomenon is thus repeated of the two groups on the same medication moving in contrary directions.

An inspection of Table VI indicates that with amphetamine sulfate, sixteen subjects in Group A improved and four were unimproved. Under the same circumstances only two improved in Group B and eighteen remained unimproved. Applying the Mann-Whitney test, $R_1$ was 270 and $R_2$ was 550. The z value was established as -3.83. This gave a $p < .01$. The third hypotheses can now be accepted: Hyperactive children will demonstrate a greater degree of emotional control, as measured by a behavioral rating scale, when administered amphetamine sulfate.

TABLE VI.

EMOTIONAL CONTROL WITH AMPHETAMINE SULFATE

| | Improved | Unimproved | Total |
|---|---|---|---|
| Group A | 16 | 4 | 20 |
| Group B | 2 | 18 | 20 |
| Total | 18 | 22 | 40 |

4. Attention Span. With the scale for "attention span" Group A had a mean measurement on the placebo of 4.09 as contrasted with a mean of 6.21 on medication. Group B had a mean score of 6.91 on placebo as against 6.10 on amphetamine. Thus the hyperactive group showed a definite movement toward a longer attention span when the medication was administered while Group B showed a trend in the opposite direction.

As tabulated in Table VII, fifteen subjects in Group A had a longer attention span when given amphetamine sulfate while five remained unimproved. Three members of Group B had a longer attention span with amphetamine and seventeen were unimproved. Application of the Mann-Whitney test with an $R_1$ of 290 and $R_2$ of 530 produced a z value of 3.41. With the $p < .01$, we now accept the fourth of the hypotheses: Hyperactive children will demonstrate a longer attention span, as measured by a behavioral rating scale, when administered amphetamine sulfate.

## C. CALIFORNIA ACHIEVEMENT TEST

The grade placements obtained from the California Achievement Test administered to the subjects provided the data for Table VIII. Group A had thirteen improved by three or more months when given amphetamine sulfate as against their performance when on the placebo. Seven were unimproved. In Group B, six showed improvement when the medication was given and eleven remained unimproved. Three subjects in Group B

TABLE VII.

ATTENTION SPAN WITH AMPHETAMINE SULFATE

| | Improved | Unimproved | Total |
|---|---|---|---|
| Group A | 15 | 5 | 20 |
| Group B | 3 | 17 | 20 |
| Total | 18 | 22 | 40 |

TABLE VIII

CALIFORNIA ACHIEVEMENT TEST RESULTS WITH AMPHETAMINE SULFATE

| | Improved | Unimproved | Total |
|---|---|---|---|
| Group A | 13 | 7 | 20 |
| Group B | 6 | 11 | 17 |
| Total | 19 | 18 | 37 |

could not be rated by this criterion. One became ill prior to testing and two were too hyperactive and distractible at one sitting to complete testing.

The Mann-Whitney test was also applied to these results. The sum of ranks provided an $R_1$ of 330 and an $R_2$ of 374. The z score was 1.54. This gave a p of .20. With this evidence we cannot accept the fifth hypothesis: Hyperactive children will demonstrate improved scholastic performance, when administered amphetamine sulfate.

At the same time there was a trend in the direction of the hypothesis. This, of course, raised the question of why some high level of confidence was not obtained as for the other four hypotheses. It was clear that this depended somewhat on the former, and it was anticipated that if the subjects were behaviorally more efficient; less hyperactive, with a longer attention span and better emotional control; they would demonstrate higher academic achievement.

A further review of the literature gave a clue that provided the examiner with what appears to be a valid explanation. The behavior being studied usually makes its appearance before the age of six (9). That means that these children have the symptamatology leading to inferior school performance prior to admission to the first grade. Thus, for the most part, they have not been able to learn and retain the material taught in the classroom. They obviously then could not reproduce on an achievement test material

which they have never ingested. For them the test of significance would seem to be whether they could learn while receiving amphetamine sulfate, the school work they had not been able to learn previously. In view of this, the examiner felt that the results were remarkably good, and the level of confidence superior to what should have been anticipated.

# CHAPTER V.

## CONCLUSIONS

The results obtained from this investigation support the major hypothesis: Hyperactive children will demonstrate more efficient behavior when administered amphetamine sulfate. This is based on the statistical evidence secured in testing these four experimental hypotheses: 1. Hyperactive children will demonstrate less gross activity, as measured by a behavioral rating scale, when administered amphetamine sulfate; 2. Hyperactive children will demonstrate less impulsive behavior, as measured by a behavioral rating scale, when administered amphetamine sulfate; 3. Hyperactive children will demonstrate a greater degree of emotional control, as measured by a behavioral rating scale, when administered amphetamine sulfate; 4. Hyperactive children will demonstrate a longer attention span, as measured by a behavioral rating scale, when administered amphetamine sulfate. A fifth hypothesis tested was that hyperactive children will demonstrate improved scholastic performance, as measured by a standard test of school achievement, when administered amphetamine sulfate. The data secured did not meet the criterion of statistical significance, although a trend in the direction of the hypothesis was noted. This could be explained in terms of the subjects being unable to produce material for the test used since they had been unable to learn it prior to the test situation.

In the broad sense, the results obtained were not in variance with but in support of the literature. Primarily it had been observed that amphetamine sulfate, unlike its stimulating effect on adults, has a sedative or inhibiting effect on some children. It has been shown to be equally true that this medication has this effect with some children and not with others. This was noted, but not explained, by some of the early observers. It has been substantiated also by experimental means that the subjects show change in many of the areas indicated in the literature. An earlier study had failed to provide conclusive proof that organicity was the differentiating criterion between those who would change in the predicted manner with amphetamine and those who would not. Yet even the writer's earlier study had indicated that in many cases those with organic cerebral dysfunction did change with amphetamine. With this research this apparent discrepancy disappears. Characteristic of many of those with an organic factor is hyperactivity. It could be expected then that the subjects in this group who were also hyperactive would change with the medication. It is thus understandable that this could lead to the hypothesis that it was organicity that differentiated between those who would and would not benefit from amphetamine. This study has extended this premise and demonstrated that not the organicity but the hyperactivity was the differential factor which allows the prediction of certain results from

the use of amphetamine sulfate. This, of necessity, includes many diagnosed as suffering from organic cerebral dysfunction.

This leaves us with the apparently contradictory information that amphetamine has an inhibiting effect on one type of child and not on another. It is around this that certain theoretical considerations are offered. It is accepted here that the human organism is a complex of psychological and physiological functions.

It should not be surprising then that the omission of the necessary psychological ingredients would have a detrimental effect upon maturation and the functioning of the central nervous system. Equally true would be the faulty ego development in those with inadequate or damaged biological structures. Extending this line of thinking, there is no reason to reject the proposition that a child may display identical symptomatology when there is either a physical lesion in some part of the central nervous system or when the psychological factors effecting this same area of the nervous system are disturbed. There is ample evidence in the literature and empirically for this, such as in idiopathic and hysterical epilepsy and the similarity in disturbance in many organic and hysterical illnesses.

This research has led the writer to believe the same process is in operation with these hyperactive children. The hyperactivity may be due to a lesion or dysfunction of the biological components, probably in the diencephalon.

On the other hand, lack of proper environmental factors in some has led to insufficient maturation and development, particularly in the cortical areas associated with control. The hyperactivity may be due to damage to the diencephalon or cortex or lack of a fully developed controlling function. Stimuli from the environment are brought through the nerve fibers to the diencephalon; the impulse to respond immediately to this stimulation is checked by control exerted by the cortex in the normal child, Group B. In Group A, no such control being present, the subjects responded with hyperactive and impulsive behavior.

Apparently, then, the attempt to utilize organicity as the criterion for the use of amphetamine sulfate is fallacious. The type of controls necessary to reduce gross activity and impulsiveness and to increase emotional control and attention span are cortical and learned, thus psychological in origin. Organicity may or may not be present, but this is incidental to the hyperactivity. It is not necessary to introduce this extraneous factor to offer a prediction for the resultant behavior produced by the administration of amphetamine sulfate to a hyperactive child.

Marazzi has pointed out (34) and Hill and Parr have confirmed (33) that amphetamine sulfate has a specific inhibiting effect on the synaptic connections at the diencephalon. Thus stimuli entering the diencephalon from the environment are slowed down and suppressed. The inhibition

provides for the hyperactive child the control which the cortex is unable to provide. The result is the more efficient behavior demonstrated when the children in Group A were given amphetamine sulfate.

The same process takes place when amphetamine is administered to non-hyperactive children, but the observed behavioral result is quite different. If amphetamine has an inhibiting action at the diencephalon, it must exert this influence on stimuli from the cortex as well as from the external environment. When this action is identical in its effect on both sources of stimulation, there should be no change in behavior. When the effect is more pronounced on the cortical connections, one could expect that these children would appear more hyperactive and the medication would appear to be acting as a stimulant. The degree of cortical control might conceivably also effect the observed results. That is, those who have a more strongly developed cortical control are less apt to show a stimulating effect from the medication than those where control and impulse are in fine balance.

The results and conclusions drawn from this investigation suggest serious thought must be given to the administration of amphetamine sulfate and point the way to additional necessary research. When amphetamine sulfate is given to a hyperactive child, it seems to provide a substitute for the lacking ego-control. The child is thus able to function without developing this ego strength and can rely on the

artificial use of medication. Does this then make learning through relationships unnecessary so that the child never gets an opportunity to mature emotionally? Can such a child develop the internal strength essential to adapt to the community? Follow-up studies on some of the hyperactive children who have received this medication over a considerable period of time might provide some of the answers. Longitudinal studies from conception to maturity might provide additional material as to what is lacking in the emotional life of those children who become hyperactive and benefit from amphetamine sulfate.

Since many of the hyperactive children eventually attract medical, psychological or psychiatric attention, the use of amphetamine sulfate as an adjunct or substitute for psychotherapy must be evaluated. There is a strong suspicion hinted at in the literature, and which this investigator felt from empirical observation, that amphetamine sulfate can interfere with psychotherapy. There seems to be such constriction of the personality and added ego control with no effort of the child, that there is little anxiety in relation to behavior and little of the prerequisite for the usual psychotherapeutic approaches. Research to examine the effects of the medication on psychotherapy would be of extreme value.

The ease of administration means that this drug can be given relatively freely by persons who do not realize all

of the implications. It thus affords an easy treatment for the busy practioner who can attain speedy symptomatic relief without effecting basic processes. Its use may be more dangerous psychologically in many cases than withholding it. On the other hand the speed with which the subject reacts to the drug, the lack of toxicity, the non-cumulative effect and the short duration of its efficacy make amphetamine sulfate quite susceptible to safe research.

# APPENDICES

# APPENDIX A

## CHILD BEHAVIOR SCALE

### Frequency of Gross Activity

The active child indulges in gross motor activity most of the time. This rating should be made on the basis of free play observation, wherein the child's preference can be observed.

Cues

Almost always engaged in gross activity, in motion.

Usually engaged in active play, such as slide, jungle gym, marching, running but is occasionally inactive during brief periods of using quiet play materials.

Child engages in gross motor activity when that type of play is called for, such as in outdoor situations. Also plays quietly when the play situation does not demand gross activity, such as in coloring, bead-stringing.

Usually engaged in quiet activity such as block play, digging in sand, etc.; occasionally joins more strenuous activities.

Extremely inactive, sedentary, stationary.

Remarks: _____

_____

_____

_____

_____

Child: _____

Observer: _____

Hours of Observation: _____

# APPENDIX B

## CHILD BEHAVIOR SCALE

### Impulsiveness

This trait refers to the patience of the child, his tendency to withhold immediate reaction for whatever reason. The child lacking this tendency is impatient; can't wait to do what he wants to do.

### Cues

Child was an extremely patient sort. Waited his turn, reserved action at will.
Only after he had waited a long time did child get impatient.

Child waited turns rather successfully, was usually patient, but under some circumstances (such as when he initiated a given group activity) was impatient.

Child occasionally demonstrated patience, occasionally deferred action but usually was off and away to execute plans.

Impetuous, impulsive child: immediately attempted execution of ideas in mind.

Remarks: _____

_____

_____

_____

_____

Child: _____
Observer: _____
Hours of Observation: _____

# APPENDIX C

## CHILD BEHAVIOR SCALE

### Emotional Control

By emotional control is meant the degree to which the child's overt expression is inhibited. Emotional expression is curbed to meet the exterior demands of the situation. The child's covert emotion may be intense; expression is inhibited.

Cues

- Child customarily controlled and restrained emotion. Very highly restrained emotionally.
- Child occasionally demonstrated outbursts of emotion (as when, tired, sleepy, etc.) but inhibited expression rather well in routine situations.
- Emotional control seemed poorly developed - frequent outbursts.
- No restraint of emotions. Reaction was prompt, frank, free.
- Never attempted to conceal expression; no inhibition.

Remarks: _____

_____

_____

_____

Child: _____

Observer: _____

Hours of Observation: _____

# APPENDIX D

## CHILD BEHAVIOR SCALE

### Attention Span

This trait is concerned with the degree to which a child maintains a persistent interest.

Cues

Child's active interest in an occupation was unusually persistent; was tenacious over long periods despite difficulty of task or presence of distraction.

Child was usually tenacious as to interest, but showed shorter attention span when upset, or when activity was much too easy or too hard.

Child's interest was usually short-lived but occasionally tenacious if the task was extremely novel or engaging.

Child's interest dwindled readily. Flitted from task to task; no persistent interest.

Remarks: _____

_____

_____

_____

_____

Child: _____

Observer: _____

Hours of Observation: _____

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# THE EFFECT OF AMPHETAMINE SULFATE UPON THE BEHAVIOR AND SCHOOL PERFORMANCE OF HYPERACTIVE CHILDREN

Abstract of a Dissertation

Submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy

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## Purpose

It was the purpose of this study to test hypotheses concerning the effects of amphetamine sulfate on certain areas of behavior and school performance of hyperactive children. The literature indicated that some children were observed to be less active and less impulsive and to have greater emotional control and a longer attention span when given amphetamine sulfate. No diagnostic criteria had been established to determine with which children this medication was effective, although many observers felt that the predicted effect occurred with children suffering from an organic cerebral dysfunction. A preliminary study by this writer to investigate the hypothesis that the administration of amphetamine sulfate to children suffering from organic cerebral dysfunction produced more efficient behavior, produced inconclusive results. It suggested that hyperactivity was the factor which differentiated between those children who would show the predicted behavioral changes with amphetamine sulfate and those who would not.

## Hypotheses and Experimental Design

The general hypothesis tested was: Hyperactive children will demonstrate more efficient behavior when administered amphetamine sulfate. Children considered hyperactive were those who consistently demonstrated a level of activity in excess of the "normal" child. More efficient behavior was considered demonstrated by a decrease in gross activity, a decrease of impulsiveness, greater emotional control, a longer attention span and improved scholastic performance. The following experimental hypotheses were utilized to test the general hypothesis:

1. Hyperactive children will demonstrate less gross activity, as measured by a behavioral rating scale, when administered amphetamine sulfate.
2. Hyperactive children will demonstrate less impulsive behavior, as measured by a behavioral rating scale, when administered amphetamine sulfate.
3. Hyperactive children will demonstrate a greater degree of emotional, as measured by a behavioral rating scale, when administered amphetamine sulfate.
4. Hyperactive children will demonstrate a longer attention span, as measured by a behavioral rating scale, when administered amphetamine sulfate.
5. Hyperactive children will demonstrate improved scholastic performance, as measured by a scholastic achievement score, when amphetamine sulfate is administered.

Independent variables were the presence or absence of hyperactivity and the administration or withholding of amphetamine sulfate. All subjects were patients at a small neuro-psychiatric hospital. Two groups were chosen by observers who regularly worked with the children. Group A consisted of twenty hyperactive children and Group B of twenty non-hyperactive children.

At two separate periods the subjects were given amphetamine sulfate or a placebo, half getting the placebo first and half the amphetamine sulfate first, and tested on each. Testing on the placebo served as a baseline for comparison. Ratings on the placebo also served as a validation of the selection of the groups. To eliminate bias, only a non-participant knew which children were on placebo or amphetamine sulfate.

Controlled variables were the setting within which the investigation took place, the subjects' familiarity with the environment, the order of testing and observation, the time of observation and the observers. The same three observers rated each child at each observation. Age and intelligence were equated.

Dependent variables were the ratings on the behavioral rating scales and the scores on the scholastic achievement test. Child behavior scales whose reliability and validity had been established at the Fels Institute were used. The California Standard Achievement Test was used to measure scholastic performance. The dependent variables were handled in terms of "improved" or "unimproved". "Improvement" referred to more efficient behavior in terms of the experimental hypotheses. The Mann-Whitney test was the statistical method of choice. A level of significance of .05 was the criterion for acceptance of the hypotheses.

Results

The reliability of the rates was calculated for Group A and Group B on amphetamine sulfate and on placebo. This was done for observation of gross activity, impulsiveness, emotional control and attention span. Correlations were similar to those at the Fels Institute.

The measurement of frequency of gross activity in Group A showed 18 improved and 2 unimproved when amphetamine sulfate was administered. In Group B none were improved. The level of significance was .01. The mean score of Group A and Group B moved in opposite directions with the administration of amphetamine sulfate.

The data gathered in measuring impulsive behavior showed that in Group A 14 improved and 6 remained unimproved. In Group B 5 improved and 15 were unimproved. The level of significance was .03. The means of the two groups were again seen to move in opposite directions with the administration of amphetamine sulfate.

Scores on the rating scale for emotional control showed that in Group A 16 improved with the administration of amphetamine sulfate and 4 were unimproved. In Group B 2 were improved, and 18 were unimproved. Significance was established at the .01 level. The means again demonstrated that the groups changed in contrary ways when amphetamine sulfate was given.

Length of attention span were also measured by the behavioral rating scales. In Group A 15 were shown to have improved and 5 were unimproved with the giving of medication. In Group B 3 improved and 17 remained unimproved. The level of significance was .01. The phenomenon of the means of the two groups moving in

opposite directions with the administration of the same medication was again observed.

On testing with the California Achievement Test 13 children in Group A improved when given amphetamine sulfate by 3 or more months and 7 did not meet this criterion. Three children in Group B could not be tested. Of the remainder 6 were improved and 11 were unimproved. The level of significance was .20.

## Conclusions

The results obtained in testing the experimental hypotheses met the criteria established in the experimental design for the first four hypotheses. The fifth did not meet the criterion but indicated a trend in that direction. It was felt that the subjects had been unable to learn the material prior to the test situation, and therefore could not reproduce it. The evidence allowed for acceptance of the general hypothesis: hyperactive children will demonstrate more efficient behavior when administered amphetamine sulfate.

The results were found to be in support of and not at variance with the literature. Amphetamine sulfate was shown to have a sedating or inhibiting effect on some children and the behavioral areas effected were those generally described in the literature. The hypothesis concerning organicity became understandable, since hyperactivity is a common characteristic of children suffering from some type of organic cerebral dysfunction. This investigation extended the premise and demonstrated that it was the hyperactivity and not the organicity which allowed for prediction. Amphetamine sulfate seems to have an inhibiting effect whether the hyperactivity is due to faulty ego development, lack of maturation or organic disease. The important factor seems to be the lack of an adequate controlling mechanism.

The results and observations indicate serious thought must be given to the use of amphetamine sulfate. It seems to provide a substitute for the lacking ego-control. Thus a child can function without adequate ego development. Without other types of therapy, this can make learning through relationships unnecessary and prevent the child from achieving emotional maturity. At the same time the ease of administration, and the swift and dramatic results with the medication make its use extremely inviting to the practitioner.

Research is suggested to determine the effects of the use of amphetamine sulfate on psychotherapy. Longitudinal studies could also be done to discover the psychological deprivations or environmental lacks which produce the observed hyperactivity. The speed with which the subject reacts to amphetamine sulfate, the lack of toxicity, the non-cumulative effect and the short duration of its efficacy make it susceptible to safe research.

Autobiography

I was born in Providence, Rhode Island, on April 11, 1916, the son of Hyman and Anna Koret. I attended the Providence public schools and graduated from Hope Street High School in 1933. In 1937 I received a B.S. degree from the University of Rhode Island where I was a member of Phi Kappa Phi, the national scholastic honor society and Tau Kappa Alpha the national debating society.

After several years conducting a laundry business, I entered the U. S. Army Air Force in May 1942. I served as a Captain in the Eighth Air Force in Europe as a bombardier and navigator. Decorations received were the Air Medal and eight oak leaf clusters, Distinguished Flying Cross and two oak leaf clusters, Distinguished Unit Medal, Croix de Guerre and Silver Star. I received my discharge in December 1945.

I was married to Alice Lecht of Providence on January 1, 1947. I then resumed my academic work at the Boston University School of Social Work and the degree of M.S. in S.S. in psychiatric social work in June 1949. Field work placements were with the American Red Cross and the Rhode Island State Hospital for Mental Diseases. I received the M.A. from Boston University in Psychology in August 1949. I then returned to the Rhode Island State Hospital as a psychiatric social worker for one year. In November 1950 I went to the Emma Pendleton Bradley Home, a neuropsychiatric hospital for emotionally disturbed children, as Chief Psychiatric Social Worker. I have also served as consultant to Crippled Children and Adults of Rhode Island and in private practice in Providence and in New Bedford. I also serve as a supervisor of psychiatric social work for Boston University and Simmons Schools of Social Work.

I have presented a paper on "Pseudo-schizophrenia" and "The Utilization of Projective Testins as a Predictor of Casework Movement" at the American Orthopsychiatric Association. Membership is held in the psychiatric division of the National Association of Social Workers, the National Conference of Social Work and the American Orthopsychiatric Association.