1-1-1977

Controversial issues concerning the treatment of hyperactive children with behavior-modifying drugs: a critical review

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CONTROVERSIAL ISSUES CONCERNING THE TREATMENT OF HYPERACTIVE CHILDREN WITH BEHAVIOR-MODIFYING DRUGS: A CRITICAL REVIEW

by

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A RESEARCH PAPER
SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF
MASTER OF ARTS IN EDUCATION
(EDUCATION OF LEARNING DISABLED CHILDREN)
AT THE CARDINAL STRITCH COLLEGE

Milwaukee, Wisconsin

1977

This research paper has been

approved for the Graduate Committee

of the Cardinal Stritch College by

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Date March 1, 1977

CONTENTS

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CHAPTER I

INTRODUCTION

The hyperactive child has been diagnosed and treated with drugs for some thirty years in the United States.[1] Recently, however, considerable controversy has appeared regarding the drugging of these children. Traditionally, hyperactivity has been defined as a symptom complex of short attention span, distractibility, impulsivity, learning difficulties, other behavior problems and "equivocal" neurological signs.[2] However, none of these terms has been objectively defined; nor have the necessary and sufficient criteria for the diagnosis been delineated as they have for say, rheumatic fevor. Inevitably, this has resulted in widely differing diagnostic practices, which in turn have lead to a great deal of criticism. The critics maintain that if physicians cannot decide on a common set of diagnostic criteria for hyperactivity they shouldn't be so willing to prescribe drugs.

The etiology or, more probably, etiologies of hyperactivity are unknown, although a number of possibilities have been suggested from

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[1]Diane Divoky and Peter Schrag, The Myth of the Hyperactive Child and Other Means of Child Control (New York: Panthem Books, 1975), p. 87.

[2]John S. Werry, "Medication for Hyperkinetic Children," Drugs 11 (November 1976):81.

perinatal brain-damage to artificial food additives.[3] These theories are all interesting but at the moment rather speculative and of little or no help in deciding treatment. This fact has also been criticized by opponents of drug therapy for children.

Another area of controversy involves the drugs themselves. Presently, there are several types of drugs which may be useful in the treatment of hyperactivity,[4] however, there is no way to predict drug response in individual children. This, plus the fact that many of the drugs being prescribed evidence abuse potential and serious side-effects, represents the oldest criticism of drug therapy practices.

Statement of Purpose

In the light of these stated areas of controversy, it was the purpose of this paper to review the literature of hyperactivity and drug therapy and to clarify some of the issues. Particular attention was paid to the description and classification and etiology of the hyperactive child; and the specific drugs presently being used to treat hyperactivity. Some specific points of controversy were also reviewed. Statements concerning the need for a practical definition of the problem, more thorough assessment of the child's behavior, and more relevant communication among involved parties were put forth in the conclusion.

Definition of Terms

Behavior-modifying drugs were seen as any chemical-pharmaceutical

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[3]Ben F. Feingold, "Hyperkinesis and Learning Disabilities Linked to Artificial Food Flavors and Colors," American Journal of Nursing 75 (May 1975):797-803.

[4]J. Gordon Millichap, "Drugs in the Management of Minimal Brain Dysfunction," Annals of New York Academy of Sciences 205 (February 1973): 321-334.

agent which, when ingested, would cause changes to occur in a child's manner of behaving in a given situation.

Hyperactivity was the term chosen as most representative and most comprehensible of some forty terms used to describe a symptom complex of short attention span, distractibility, impulsivity, learning difficulties, other behavior problems, and equivocal neurologic signs in children.

Summary

Much controversy concerning the use of behavior-modifying drugs in treating hyperactivity has become evident in recent years. This controvesy centers on problems inherent in describing and classifying the "problem" children; and on the possible dangers of prescribing drugs for their treatment.

The present paper reviewed the literature of drug therapy for hyperactivity with the purpose of clarifying some of the major issues. Statements concerning the need for a practical definition of the problem, more thorough assessment of the behaviors, and more communication among professionals were also presented.

CHAPTER II

REVIEW OF THE LITERATURE

Terminology

The confusion of terminology applied to hyperactivity is evident when one considers that since 1934 some forty names have been used to describe the same syndrome.[1] The fact that many of these terms are still applied only helps to sustain the confusion. Some of the more familiar names that have been used include organic driveness, postencephalitic behavior disorder, hyperkinesis, hyperactivity, the hyperactive child syndrome, minimal brain damage, minimal brain dysfunction, minimal cerebral dysfunction, specific learning disability, brain-injured child, and hyperkinetic impulse disorder.[2]

Classification and Definition

The profusion of terminology offers some evidence of the confusion that has affected the classification or definition of hyperactive children. Historically a pattern in the classification can be seen. In general, the classification of hyperactive children has proceeded from a homogeneous

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[1] Divoky and Schrag, Myth, p. 41.

[2] E. Kahn and L. Cohen, "Organic Driveness: A Brain Stem Syndrome and Experience," New England Journal of Medicine 210 (April 1934):748-756; Wender, "Minimal Brain Dysfunction Syndrome," p. 45; Alfred A. Strauss and Laura E. Lehtinen, Psychopathology and Education of the Brain-Injured Child, 2 vols. (New York: Grune & Stratton, 1947-55). vol. 1; Maurice W. Laufer, Eric Denhoff, and Gerald Solomons, "Hyperkinetic Impulse Disorder in Children's Behavior Problems," Psychosomatic Medicine 19 (February 1957): 38-49.

medical classification (e.g. Strauss),[3] to a more heterogeneous (e.g. Wender)[4] description. Presently, some researchers are suggesting the possibility of a number of classifications for the same syndrome based on etiological factors.[5]

The first connection between classroom behavior and possible neurological problems may have occurred in 1934 in an article in the New England Journal of Medicine. The article, entitled "Organic Driveness: A Brain Stem Syndrome and Experience," tells of a behavioral syndrome involving distractibility, short attention span, impulsivity, and poor coordination which often times accompanied encephalitis, but which could also be seen in people with no known brain damage or illness. The authors chose to label the syndrome "organic driveness." They concluded that it was medically determined by some dysfunction of the central nervous system.[6]

In 1947 Alfred A. Strauss, the director of a school of brain-damaged children (most of whom exhibited severe signs of pathology) reported that such children exhibited distinctive behaviors, including hyperactivity, which could be traced to injuries or diseases during the perinatal period.[7] This concept was expanded in 1955 by Strauss and Newell C. Kephart. They concluded that certain "so-called 'normal' brain-injured children,"

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[3]Alfred A. Strauss and Newell C. Kephart, Psychopathology and Education of the Brain-Injured Child, 2 vols. (New York: Grune & Stratton, 1947-55), vol. 2: Progress in Theory and Clinic, p. ix.

[4]Wender, "Minimal Brain Dysfunction Syndrome," pp. 45-52.

[5]Philip G. Ney, "Four Types of Hyperkinesis," Canadian Psychiatric Association Journal 19 (December 1974):543-550; Barbara K. Keogh, "Hyperactivity and Learning Disorders: Review and Speculation," Exceptional Children 38 (March 1971):101-109.

[6]Kahn and Cohen, "Organic Driveness," p. 754.

[7]Strauss and Lehtinen, Psychopathology, vol. 1, p. 4.

demonstrated behaviors and learning problems similar to children with known organic damage. The 1955 children exhibited no specific organic damage and there was no history of perinatal trauma.[8] The conclusions were based entirely on inferences drawn from behaviors. The children described thus far remained somewhat homogeneous in their problems and their classification. However, in 1957 Maurice Laufer presented his description of a new syndrome: "hyperkinetic impulse disorder." Hyperactivity was noted as the most striking item, with short attention span and poor powers of concentration, "which are particularly noticeable under school conditions." He also states that the child is impulsive, irritable and explosive and manifests a low frustration tolerance. These behavioral characteristics "make it very difficult for the child to participate in the work of a school room."[9]

Laufer's description essentially did two things: 1) it related hyperactivity ("hyperkinetic impulse disorder") directly to the classroom; and 2) made it possible to include any number of children with non-specific classroom problems into a special group. The bandwagon, as it were, was rolling.

So many jumped on it that by 1963 The National Institute of Blindness and Neurological Diseases assembled a Task Force comprised of physicians to report on terminology and identification of the syndrome. In its report, the Task Force decided on the term "minimal brain dysfunction" and described it as follows:

> Minimal brain dysfunction syndrome refers in this paper to children of near average, average, or above average general intelligence with certain learning or behavioral disabilities ranging from mild to severe, which are associated with deviations of function of the central nervous system. These deviations

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[8] Strauss and Kephart, Psychopathology, vol. 2.

[9] Laufer, "Hyperkinetic Impulse Disorder," p. 38.

> may manifest themselves by various combinations of impairment in perception, conceptualization, language, memory, and control of attention, impulse, or motor fuction.[10]

In clarifying the problem, the Task Force simply seemed to add to the already existing confusion. For example in discussing possible etiology the monograph states:

> These aberrations may arise from genetic variations, biochemical irregularities, perinatal brain insults or other illnesses or injuries sustained during the years which are critical for the development and maturation of the central nervous system, or from unknown causes.[11]

Werry states that none of the "so-called CNS deviations have yet established themselves as valid or reliable indices of cerebral functioning in the neurological sense."[12] This statement is supported by Birch.[13]

The monograph goes on to describe a list of the syndrome's most prevalent symptoms. It presents ninety-nine, including: "achievement low in some areas, high in others"; "hyperkinesis"; or "hypokinesis"; "poor spatial orientation"; "poor printing, writing, or drawing ability" and ninety-four more.[14] Indeed, it became difficult to find children who didn't fit into the Task Force's definition, and what began as an effort to clarify a problem actually created more confusion.

John S. Werry, in his criticism of the Task Force's report, felt that

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[10]Sam D. Clements, ed., Task Force I: Minimal Brain Dysfunction in Children: Terminology and Identification, National Institute of Neurological Diseases and Blindness, Monograph No. 3, U.S. Department of Health, Education and Welfare (Washington, D.C.: U.S. Government Printing Office, 1966), pp. 6-7.

[11]Ibid., pp. 9-10.

[12]John S. Werry, "Studies on the Hyperactive Child," Archives of General Psychiatry 19 (July 1968):9.

[13]Harold G. Birch, Brain Damage in Children: The Biological and Social Respects (New York: Williams and Wilkins Co., 1964), pp. 3-12.

[14]Divoky and Schrag, Myth, pp. 44-45.

the tendency had been "to classify the dysfunction on an a priori or logical basis."[15] He suggested factor analysis as an alternative way to empirically delineate the dysfunction. In an experiment, he subjected to factor analysis a number of neurological, EEG, medical history, cognitive, and psychiatric measures taken on 103 hyperactive children of normal intelligence. His principal findings were as follows:

> ...There is a very low degree of interrelatedness between neurological, cognitive, behavioral, medical-historical, and EEG dysfunction suggesting perhaps that each is a reflection of different etiological factors. Certainly the existence of a homogeneous "brain damage" dimension in its simplist sense is refuted by this...[16]

A 1972 study by Conners seems to support Werry's conclusion.[17] Noticing some inconsistencies in a series of studies conducted by himself and his associates, Conners selected 178 previously treated subjects and, based on pre- and post-drug measuring instruments, developed a profile analysis in order to achieve as much diagnostic homogeneity as possible. He found that the group could be distinguished in terms of seven different patterns of baseline performance. He also discovered that their response to stimulant drugs differed widely and depended on their initial profile of abilities. All those in Conners' sample had been diagnosed as minimal brain dysfunction in accordance with the official definitions. However, the group proved to be heterogeneous in its profiles, and changes due to drug therapy differed accordingly. Conners suggests that there is "no single syndrome of hyperkinesis which is uniquely responsive to drug

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[15]Werry, "Studies," p. 9.

[16]Ibid., p. 15.

[17]C. Keith Conners, "Symposium: Behavior Modification by Drugs - II: Psychological Effects of Stimulant Drugs in Children With Minimal Brain Dysfunction," Pediatrics 49 (May 1972):702-708.

therapy."[18]

The studies by Werry and Conners made it exceedingly difficult for physicians to maintain that one kind of brain syndrome was responsible for hyperactivity in children. Another approach was needed in the classification and definition of these children. Some researchers found this new approach by relating specific cases to etiological factors.

Solomons, in 1967, listed four possible etiological categories. They were: 1) constitutional activity level; 2) immaturity; 3) emotional disturbance; and 4) diffuse brain damage. He described constitutional activity level hyperactivity as a relative inconsistency between the child's normal behavior level and that expected of him/her by parents or teachers. Depending upon the situation, this child's behavior is seen as variable. Hyperactivity due to immaturity may be "tentatively suggested when the overall picture is that of a child whose behavior appears to be one or more years below his age level, with no gross signs of neurological impairment, and no major problems evident." Gradual improvement will also be noted in these cases. Those children suffering hyperactivity resulting from emotional disturbance will demonstrate "no gross neurological deficiences, no gross intellectual impairment or perceptual problems; but there is a history conducive to emotional upset."[19] Solomons believes that psychiatric or psychological testing will confirm this diagnosis. In describing hyperactivity due to diffuse brain damage, a major weakness is noted in Solomons approach. He states:

> A specific syndrome of behavior characterized by chronic, severe hyperactivity without gross neurologicall defects, has

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[18]Ibid., p. 706.

[19]Gerald Solomons, "Child Hyperactivity: Diagnosis and Treatment," Texas Medicine 63 (November 1967):52-57.

> been seen to occur after head injury, epidemic encephalitis, communicable disease encephalopothies in children and sometimes without a preceding significant history. This has been called the "hyperkinetic syndrome" by Werry and others . . .[20]

From here Solomons goes on to describe the exact syndrome which percipitated his suggesting an etiological approach to classification and definition of the hyperactive child. He also maintains, as a final note, that drug therapy is not used enough, but he makes no distinction about which of his categories of hyperactive children should or should not receive drugs. Is it, after all, necessary to drug a child whose behavior simply doesn't conform relative to certain adults' expectations?

Schmidt, et al., 1973, also listed four possible etiological categories to explain hyperactivity in children. These were: 1) neurological hyperactivity of which there were two types: minimal cerebral dysfunction, a chronic and static condition; and cerebral deterioration, an acute and progressive condition; 2) mental retardation; 3) developmental hyperactivity; and 4) psychogenic hyperactivity also evidencing two types, mild and severe. Mild psychogenic hyperactivity was said to be situational, and might be caused by parental overreaction to one of the other types. Severe psychogenic hyperactivity was related to maternal deprivation, psychosis, and severe neurosis.[21]

Block in 1974, offered five etiological categories in which to classify children designated as having "minimal brain damage." These were: 1) organic brain damage, including only those children who demonstrate measureable neurologic deficits; 2) hyperkinetic behavior syndrome

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[20]Ibid., p. 53.

[21]Barton D. Schmidt et al., "The Hyperactive Child," Clinical Pediatrics 12 (Philadelphia: J.B. Lippincott Company, March 1973), pp. 154-169.

("children whose main problem is their overactive behavior"); 3) specific learning disability or dyslexia ("the child who has significant deficits in his learning ability in spite of normal intellectual potential and absence of sensory, motor, or emotional handicaps"); 4) maturational lag, includes children who demonstrate evidence of developmental immaturity; and 5) vague cerebral dysfunction.[22] It is with this fifth category that Block's intentions become confusing. He effectively argues that the term "minimal" should be replaced by the term "vague," but he neglects to demonstrate how this group is significantly different from the other four except to say that these children are sometimes called "emotionally disturbed."[23]

In 1971 Keogh deduced three possible etiological classifications for childhood hyperactivity. Some children, she stated, may be demonstrating one aspect of "a basic impulse habit pattern." These pupils are likely to make hasty decisions and do poor school work. In new uncertain learning areas they may demonstrate heightened eye and body movement. In other children, hyperactivity may simply reflect "information seeking" among those who are limited in intelligence. Finally, Keogh suggests that hyperactivity may be the result of a measurable neurological impairment. It is concluded that children who demonstrate this type of hyperactivity should be drugged.[24]

Using sixty children considered to be hyperactive by parents or teachers, Ney was able to group them into four etiological categories. The groups were termed constitutional, behavioral, chemical, and chaotic.

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[22]Walter M. Block, "Cerebral Dysfunctions - Clarification, Deliniation, Classification," Behavioral Neuropsychiatry 5 (March 1974): 13-17.

[23]Ibid., p. 15.

[24]Keogh, "Hyperactivity and Learning Disorders," pp. 102-107.

Constitutional hyperactivity was described as being "due to either a sex-linked genetic transmission or to an extreme biological variation." This child, it is suggested, will demonstrate greater difficulty in school than at home.[25]

Behavioral or conditioned hyperactivity is the result of a child's not receiving positive reinforcement for quiet behavior from a depressed mother. This child will usually be seen or hyperactive only at home and may be reported as "quiet and conscientious" in school.

Ney sees the chemical hyperactive child having low concentrations of monoamines (impulse transmitting substance) at the diencephalon (brain stem area), thus causing the brains of these children to be relatively deprived of stimulus. He states that: "The chemical hyperactive child must then engage more actively with the environment to provoke more auditory and visual stimuli." These children demonstrate a high degree of hyperactivity in all situations.

Chaotic hyperkinesis may be a child's response to inconsistencies in parental discipline. Nightmares and hallucinations were found to be common with these children, as were devious behaviors like lying and stealing.[26]

Ney recommends psychotherapy as treatment for constitutional, behavioral, and chaotic hyperactive children. Family and school counseling are also suggested and in the case of some chaotic hyperactives, he suggests temporary removal from the home. Only with the chemical hyperactive does he recommend drug treatment.[27]

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[25]Ney, "Four Types," pp. 544-545.

[26]Ibid., pp. 547-548.

[27]Ibid., pp. 548-549.

In December 1975 Susan Stephenson listed eleven "underlying causes" for hyperactivity. They were:

> 1) The normal two to 3 year old child, who has the high activity level appropriate to this developmental phase;
> 2) The retarded child with a mental age of two to three years;
> 3) The child with a constitutionally high activity level, particularly where the child's activity level is not appreciated by parents, teachers or other important adults;
> 4) The child whose normal activity is restricted at home or in the classroom;
> 5) The child who is bored or frustrated in school;
> 6) The "no breakfast syndrome"...(irritability, lack of concentration, due to low blood sugar);
> 7) The unsocialized child, who comes from a family which is chaotic and disorganized. The children are never taught to curb impulses, delay gratification or control behavior;
> 8) The anxious child. Restlessness and inattentiveness are sometimes manifestations of anxiety in children;
> 9) The true hyperkinetic child as described in The British Studies, where the child exhibits continuous, non-goal directed motion in all situations;
> 10) The autistic child who is often overactive; and
> 11) Unusual causes, e.g., hyperthyroidism, lead poisoning.[28]

It seems that the trend in classification of hyperactive children by etiological definition is running into the same problems that Clements' clarification of the issue did. It is becoming difficult to find children who don't fit into some etiological category, especially those categories that lend themselves to relative interpretations by adults, e.g., constitutional, unsocialized, bored or frustrated.

Though there still appears to be support for defining or classifying hyperactive children by etiology, some medical researchers, notably Paul Wender, feel that the term minimal brain dysfunction syndrome is adequate if its characteristics are clearly stated and understood.

Wender believes that children suffering minimal brain dysfunction (MBD) demonstrate major dysfunctions in the areas of behavior and perception and

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[28]P. Susan Stephenson, "What is a Hyperactive Child?" Canada's Mental Health 23 (December 1975):5.

cognition. This review, however, in dealing specifically with hyperactivity, will limit itself to a discussion of dysfunctions in the area of behavior, which include motor behavior, attentional difficulties, and impulse control, as stated by Wender.

Wender sees increased levels of activity and impaired coordination as the most characteristic alterations of motor behavior in MBD children. He feels, however, with regard to the former, "that MBD children are not universally excessively active but that their activity is inappropriate." Impaired motor coordination may be seen in fine motor performance, hand-eye coordination, and balance.[29]

According to Wender, attentional difficulties are present "in most, if not all," MBD children and probably occur along a continuum:

> Many children fail to display the eager interest in school subjects which their teachers would wish. The question is again one of degree. In clear-cut instances of MBD, teachers and tutors will report that the child is able to stay with his work only when he receives constant one-to-one attention and reinforcement.[30]

Wender thinks that the most distressing characteristic of MBD is an impairment of impulse control. This may be seen most often as age-related. The toddler who is difficult to toilet train, the school-age child who has difficulty restraining him/herself from activities like playing with matches and the adolescent who performs acts of delinquency or sexual acting-out are all demonstrating impairments of impulse control according to Wender.[31]

It can be seen that analyzing and describing the characteristics of hyperactive children still leaves much confusion and uncertainty regarding

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[29]Wender, "Minimal Brain Dysfunction," p. 45-46.

[30]Ibid., p. 47.

[31]Ibid., p. 48.

diagnosis. Certainly not all adolescents who perform delinquent acts are hyperactive, and just because a child may not be an eager learner is no reason to diagnose MBD and give a drug. How then can a medical diagnosis of hyperactivity or MBD be made? Stephen, Sprague and Werry believe that only "those children whose acitivity is two standard deviations above a group of similar age, sex, and cultural backgrounds, and who do not have evidence of brain damage," should be diagnosed as hyperactive. They point out, however, that since there are no norms establishing the amounts of activity of children, that this would be difficult.[32] Wender believes that if MBD is suspected, the child should be given a drug for a trial period. If the response is seen as an improvement, then it could be concluded that the child does, indeed, have MBD.[33] Wender's reasoning is very sound, given the confusion and lack of specificity concerning this syndrome, and given that all reasoning to this point has been correct. There are many who believe it hasn't.

For example, Divoky writes:

> The learning disabilities movement takes its doctrine from a primitive body of medico-educational theory, updated and extended to meet the political and social necessities of an age searching desperately for an explanation to a classic problem and for a scientific replacement for the golden rule and the hickory stick.[34]

H.H. Comly feels that the term "dysactivity" should be used instead of hyperactivity, to indicate not too much activity, but rather the wrong kind as judged by teachers and parents.[35] Francis Crinella stated that the

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[32]Kenneth Stephen, Robert L. Sprague, and John S. Werry, Detailed Progress Report of Grant MH18909, University of Illinois (1973):1-13.

[33]Wender, "Minimal Brain Dysfunction," p. 53.

[34]Divoky and Schrag, Myth, p. 37.

[35]Harold Comly, "Cerebral Stimulants for Children with Learning Disorders," Journal of Learning Disabilities 4 (October 1971):20-26.

only thing known about the children who are classified as hyperactive is that they are all very dissimilar.[36]

In a most comprehensive review of the research literature concerning treating children with stimulant drugs, Stroufe and Steward wrote:

> The concept of "minimal brain dysfunction" has now become widely accepted, even though the reasoning behind it is often circular--that is, authors have assumed that behaviors such as hyperactivity were signs of brain damage independent of neurologic indexes, and, therefore, that many behavior problem children had brain damage. Moreover, a positive response to stimulant drugs has been used as a confirmation of the diagnosis of organicity. However, when hyperactivity and minimal brain dysfunction are defined simply as clusters of difficult behaviors, only a small minority of such children seem to have had brain damage.[37]

The lack of agreement and confusion evident in the literature certainly indicates the need for physicians to re-evaluate their diagnostic procedures in assessing hyperactivity.

The confusion and controversy associated with classifying and defining hyperactive children is not unique to medicine. Educators have developed their own terminology and numerous classification systems. However, educators cannot prescribe drugs, so for the purpose of this paper, no discussion of educational definitions and classifications was warranted.

Etiology

Discussions of etiological factors associated with hyperactivity are equally as controversial and confusing as the problem of classification and definition. Recently, several investigators have questioned the traditionally accepted belief that hyperactivity is a result of brain dysfunction. In

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[36]Francis Crinella, Frances W. Beck, and James Robinson, "Unilateral Dominance is Not Related to Neuropsychological Integrity," Child Development 42 (March 1971):2033-2054.

[37]L. Alan Stroufe and Mark A. Stewart, "Treating Problem Children with Stimulant Drugs," New England Journal of Medicine 289 (April 1973):408.

well-controlled studies conducted in 1973 and 1974, researchers found evidence indicating that hyperactivity may indeed not be related to a manifestation of subclinical or minimal brain damage.[38]

Others have suggested that hyperactivity is innate. Some studies have attempted to show that it is an inherited characteristic. Willerman found that activity level is highly correlated in monozygotic twins, while in dizygotic twins it isn't.[39] Safer, in 1973, found that ten of nineteen full siblings of hyperactive children were considered to be hyperactive as opposed to only two of twenty-two half siblings.[40] In 1975 Cantwell suggested that hyperactivity was the result of "polygenic inheritance." This means that "more than one gene is involved in the transmission of a disorder and a proband manifests the disorder only when the correct number or combination of genes are present."[41] Cantwell further indicates that because of the complexity of this process, it is very difficult to prove or disprove.[42] This seems consistent with most of the literature related to hyperactivity.

An increased frequency of minor physical anomalies including epicanthal

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[38]Donald Shaffer, Nancy McNamara, and John H. Pincus, "Controlled Observations on Patterns of Activity, Attention and Impulsivity in Brain-Damaged and Psychiatrically Disturbed Boys," Psychological Medicine 4 (January 1974):4; L.W. Talkington and W.O. Hutton, "Hyperactive and Non-Hyperactive Institutionalized Retarded Residents," American Journal of Mental Deficiencies 78 (January 1973):47.

[39]Lawrence Willerman, "Activity Level and Hyperactivity in Twins," Child Development 44 (October 1973):288.

[40]Daniel J. Safer, "A Familial Factor in Minimal Brain Dysfunction," Behavioral Genetics," (Summer 1973):175-186.

[41]Dennis P. Cantwell, "Genetics of Hyperactivity," Journal of Child Psychiatry 16 (July 1975):262.

[42]Ibid., p. 263.

folds, hyperteliorism, low set and malformed ears, high-arched palate, short incurving fifth finger, strabismus, and even skull circumferences outside the range of normal limits have been associated with hyperactivity.[43]

Coleman found a low concentration of platelet serotonin in children who demonstrated symptoms of hyperactivity without classical evidence of neurologic dysfunction.[44] This is consistent with Wender's hypothesis that hyperactivity results from a deficiency of monoamines in the diencephalon.[45] (Serotonin is one of the monoamines, the others are dopamine and norepinephrine.)

A number of researchers have suggested that hyperactivity might be lead-induced. Oliver and Clark in 1972 and Oliver in 1974 investigated and found an association between low level lead concentrations in the body and hyperactivity in children. Silbergeld and Goldberg found that mice subjected to lead in drinking water were more than three times as active as age-matched or size-matched controls.[46]

Other nutritional deficiencies have been suggested as causing hyperactivity also. Walker linked hyperactivity to low blood glucose

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[43]Wender, "Minimal Brain Dysfunction," p. 52.

[44]Mary Coleman, "Serotonin Concentrations in Whole Blood of Hyperactive Children," Journal of Pediatrics 78 (June 1971):985-990.

[45]Paul H. Wender et al., "Urinary Monoamine Metabolites in Children with Minimal Brain Dysfunction," American Journal of Psychiatry 127 (January 1971):147-151.

[46]Donald J. Oliver, "Association Between Lower Level Lead Concentrations and Hyperactivity in Children," Environmental Health Perspectives 7 (August 1974):17; Donald Oliver, Janice Clark, and Karen Voeller, "Lead and Hyperactivity," Lancet 2 (February 1972):900; Ellen K. Silbergeld and A.M. Goldberg, "Pharmacological and Neurochemical Investigations of Lead-Induced Hyperactivity," Neuropharmacology eds., P.B. Bradley and E. Costs (Oxford: Pergamon Press, 1975):431.

concentrations.[47] Hoffer thinks that excessive intake of refined white sugar and a lack of vitamins effects the activity level of youngsters.[48]

Shaffer, McNamara, and Pincus suggested that hyperactivity is a manifestation of a psychiatric disorder rather than of an abnormality of the central nervous system. It was found that mothers' reports of overactivity, tallied with a measure of disturbance of conduct and not with objective measures of activity or inattention.[49] McNamara found a link between hyperactivity and "apartment-bound" children, especially in overcrowded or ghetto neighborhoods.[50]

Denson, Nanson, and McWatters indicate a connection between hyperactivity and maternal smoking during pregnancy.[51]

Finally, a great deal of attention has lately been paid to the idea that food additives, namely, artificial coloring and flavoring, may be a significant causative factor in hyperactive behavior. Dr. Ben Feingold is the leading proponent of this theory but he has gotten some support from others.[52] One certainly doesn't get the impression of any clear-cut cause of hyperkinesis.

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[47]Sydney Walker, "Drugging the American Child: We're too Cavalier About Hyperactivity," Journal of Learning Disabilities 8 (June/July 1975):354-358.

[48]Andrew Hoffer, "Last Words on the Subject," British Columbia Medical Journal 17 (May 1975):6.

[49]Shaffer, McNamara, and Pincus, p. 7.

[50]John J. McNamara, "Hyperactivity in Apartment-Bound Child," Clinical Pediatrics 11 (Philadelphia: J.B. Lippincott Company, 1972):371.

[51]R. Denson, J.L. Nanson, and M.A. McWatters, "Hyperkinesis and Maternal Smoking," Canadian Psychiatric Association Journal 20 (April 1975): 183-187.

[52]Ben F. Feingold, "Hyperkinesis and Learning Disabilities Linked to Artificial Food Flavors and Colors," American Journal of Nursing 75 (May 1975):797-802; Sushma Palmer, Judith L. Rapoport, and Patricia Q. Quinn, "Food Additives and Hyperactivity," Clinical Pediatrics 14 (Philadelphia: J.B. Lippincott Company, 1975):956-959.

The Drugs

The question of which drug to prescribe for hyperactivity appears to be as perplexing as the questions of terminology, classification and definition, and etiology already discussed. Gerald Solomons wrote:

> Once the decision to initiate drug therapy is made, the choice of the drug is important. A large armamentarium ranges from the psychostimulants to tranquilizers, antidepressants, and antihistamines. The drug choice can often be determined by the behavior itself . . . In many instances, the appropriate drug is arrived at only by trial and error.[53]

In 1976 John S. Werry wrote:

> The hyperkinetic syndrome is a symptom complex of hyperactivity, short attention span, distractibility, learning difficulties, other behavior problems, and "equivocal" neurological signs. However, none of these terms has ever been objectively defined and at present diagnosis is largely a matter of clinical judgement. In the management of the disorder, drugs do have a place, but the decision to use medication is a complex procedure diagnostically and therapeutically calling for the highest in clinical skill and medical supervision.[54]

In view of the complex nature of drug administration and prescription for hyperactivity this section of the present paper examined some of the "large armamentarium" of available drugs. Also, since it appeared that stimulants were the drugs of choice of most physicians[55] some of the literature relating specifically to their use was reviewed.

According to Werry there are five general categories of drugs from which physicians have selected specific agents. These are the stimulants,

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[53]Gerald Solomons, "Drug Therapy: Initiation and Follow-up," Annals of New York Academy of Sciences 205 (February 1973):338.

[54]John S. Werry, "Medication for Hyperkinetic Children," Drugs 11 (May 1976):81.

[55]John M. Krager and Daniel Safer, "Type and Prevalence of Medication Used in the Treatment of Hyperactive Children," New England Journal of Medicine 291 (November 1974):1119; J. Gordon Millichap, "Drugs in the Management of Minimal Brain Dysfunction," Annals of New York Academy of Sciences 205 (February 1973):321.

the antipsychotics, tricyclic antidepressants, antihistamines, and lithium salts.[56] One other category, anticonvulsants was discussed by Millichap.[57]

Antipsychotics

These used to be called major tranquilizers. Goodman and Gilman refer to them as psychotherapeutic drugs and report that they account for twenty percent of all prescriptions in an average community.[58] This group of drugs includes chlorpromazine (Thorazine); reserpine (Serpasil); thioridazine (Mellaril); and chlordiazepoxide (Librium) which have been reported in the treatment of hyperactivity.[59] Hydroxyzine (Atarax) and haloperidol have also been used in treating hyperactivity.[60]

In general, the antipsychotics have been found to be useful in treating hyperactivity. Thioridazine has been primarily used in the treatment of mentally retarded children who are hyperactive. Millichap reported that of 308 children treated, fifty-seven percent were benefited and only two percent experienced side effects, mainly drowsiness.[61] Sprague, Barnes, and Werry found that, when used with emotionally disturbed boys, the positive effects of thioridazine were greater than placebo, but significantly

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[56]Werry, "Medication," pp. 83-85.

[57]Millichap, "Drugs," p. 329.

[58]Louis M. Goodman and Alfred Gilman, The Pharmacological Basis of Therapeutics, 5th ed., (New York: MacMillan Publishing Co., Inc., 1975), p. 152.

[59]Millichap, "Drugs," pp. 328-329.

[60]Lawrence M. Greenberg, Mary Ann Deem, and Steven McMahon, "Effects of Dextroamphetamine, Chlorpromazine, and Hydroxyzine on Behavior and Performance in Hyperactive Children," American Journal of Psychiatry 129 (November 1972):532-539; Marjorie G. Aman and John S. Werry, "The Effects of Methylphenidate and Haloperidol on the Heart Rate and Blood Pressure of Hyperactive Children with Special Reference to Time of Action," Psychopharmacologia 43 (Berlin: Springer Verlag, 1975):163-168.

[61]Millichap, "Drugs," p. 328.

less than methylphenidate (Ritalin).[62]

Millichap indicated that in trials with 237 children with hyperactivity and other behavior disorders (not stated), sixty percent showed improvements while using chlordiazepoxide.[63] Chlorpromazine was demonstrated to have beneficial effects in an average of fifty-five percent of 153 children treated. However, side effects occurred more frequently with chlorpromazine than with other antipsychotics.[64] Also, there has been at least one report of hyperkinesis due to the use of chlordiazepoxide.[65]

Greenberg, Deem, and McMahon found in a study of sixty-one hyperactive children that chlorpromazine and dextroamphetamine (Dexedrine) were equally effective, but chlorpromazine produced fewer side-effects than dextroamphetamine.[66] They also found that hydroxyzine was significantly less effective than either dextroamphetamine or chlorpromazine.[67]

In studies on twenty-four hyperactive children, Werry and Aman report comparable small effects facilitating performance with methylphenidate and haloperidol in small doses. However, there was some suggestion that higher doses of haloperidol might cause a slight deterioration in performance

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[62]Robert L. Sprague, Kenneth R. Barnes, and John S. Werry, "Methylphenidate and Thioridazine: Learning, Reaction Time, Activity, and Classroom Behavior in Disturbed Children," American Journal of Orthopsychiatry 40 (July 1970):623.

[63]Millichap, "Drugs," p. 328.

[64]Ibid., p. 529.

[65]G. P. Maguire, R.C.B. Aitken, and A.K. Zeally, "Hyperkinesis Due to Chlordiazipoxide," Journal of International Medical Research 1 (January 1972):15.

[66]Greenberg, Deem, and McMahon, pp. 533-535.

[67]Ibid., p. 537.

related to attention and cognition.[68]

Tricyclic Antidepressants

Imipramine is presently the only tricyclic antidepressant reported in the literature of drugs and hyperactivity. Imipramine (Tofranil) and other closely related compounds are reported by Goodman and Gilman as the drugs most commonly used for the treatment of depression. It has also proven effective in treating enuresis.[69] No mention is made concerning its use in treating hyperactive children.

Rapoport, in 1965, reported improvement in alertness, handwriting, reading, and arithmetic in children suffering behavior disorders from temper tantrums to delinquency when they were treated with imipramine.[70] Gross stated that imipramine was an extremely effective drug in the treatment of minimal brain dysfunction, especially where methylphenidate and dextro-amphetamine proved ineffective.[71] Gittelman-Klein reported that high doses of imipramine were relatively well-tolerated and that "methylphenidate is not regularly efficacious where imipramine fails.[72]

Several studies strongly refute Gittelman-Klein's assertion that high doses of imipramine are relatively well-tolerated. Claims of seizures,

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[68]Marjorie G. Aman and John S. Werry, "Methylphenidate and Haloperidol in Children: Effects on Attention, Memory, and Activity," Archives of General Psychiatry 32 (April 1975):793.

[69]Goodman and Gilman, p. 174.

[70]Judith Rapoport, "Childhood Behavior and Learning Problems Treated with Imipramine," International Journal of Neuropsychiatry 1 (July 1965); 635.

[71]Mortimer D. Gross, "Imipramine in the Treatment of Minimal Brain Dysfunction," Psychosomatics 14 (September 1973):285.

[72]Rita Gittelman-Klein, "Pilot Clinical Trial of Imipramine in Hyperkinetic Children," Clinical Use of Stimulant Drugs in Children, ed., C. Keith Conners (New York: American Elsevier Publishing Co., Inc., 1975): 200.

cardiotoxic effects, and one instance of sudden death in a seven year old girl are reported in connection with high doses of imipramine.[73] Hayes, Panitch and Barker state that, as a result of cardiotoxic effects, the Federal Drug Authority has limited the maximum daily dosage of imipramine to 5 mg/kg daily for children.[74]

Antihistamines and Anitconvulsants

Other drugs, excluding stimulants, which have been used in the treatment of hyperactivity include lithium carbonate, dephenhydramine (Benadryl), diphenylhydantoin (Dilantin), and primidone (Meysoline). Diphenhydramine is an antihistamine; dephenylhydantoin and primidone are anticonvulsants.[75]

Lithium carbonate, according to Goodman and Gilman is effective in the treatment of the manic phase of manic-depressive illness, and as a mood stabilizing drug.[76] Its usefulness in treating hyperactive children has not yet been established. Whitehead and Clark reported that there was "no difference between the activity level and behavior occuring with lithium carbonate intake and that occurring with placebo intake.[77] Greenhill et al.

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[73]David Brown et al., "Imipramine Therapy and Seizures: Three Children Treated for Hyperactive Behavior Disorders," American Journal of Psychiatry 130 (February 1973):210-212; Bertrand Winsberg, et al., "Imipramine and Electrocardiographic Abnormalities in Hyperactive Children," American Journal of Psychiatry 132 (May 1975):542-545; Kenneth Sarat et al., "Imipramine and Side-Effects in Children," Psychopharmacologia 37 (New York: Springer-Verlag, 1974):265-274.

[74]Thomas Hayes, Martha L. Panitch, and Eileen Barker, "Imipramine Dosage in Children: A Comment on 'Imipramine and Electrocardiographic Abnormalities in Hyperactive Children,'" American Journal of Psychiatry 132 (May 1975):546-547.

[75]Millichap, "Drugs," pp. 329-330.

[76]Goodman and Gilman, p. 184.

[77]Paul Whitehead and Lincoln D. Clark, "Effect of Lithium Carbonate, Placebo, and Thioridazine on Hyperactive Children," American Journal of Psychiatry 127 (December 1970):124.

reported similar findings.[78]

The anticonvulsants, drugs used in the treatment of epilepsy, have produced positive effects in hyperkinetic children who demonstrated seizures.[79] Pasamanick found that phenylhydantoin was relatively ineffective in the control of hyperactive behavior.[80] Millichap et al. found, however, that phenylhydantoin was valuable in treating auditory-perceptual deficits in a study of twenty-two children with learning and behavior disorders.[81] Millichap reported that the antihistamine diphenhydramine is sometimes advocated, but Conners questions its effectiveness.[82]

Stimulants

The drugs most often prescribed for the treatment of hyperactivity are the stimulants. These include methylphenidate hydrochloride (Ritalin), dextroamphetamine (Dexedrine), racemic amphetamine (Benzedrine), levo-amphetamine (Cybil), deanol (Deaner), and pemoline (Cylert). However, before examining these drugs individually, a short general review of why they are so popular is warranted.

The therapeutic use of stimulants in the treatment of hyperactivity

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[78] Laurence Greenhill et al., "Lithium Carbonate in the Treatment of Hyperactive Children," Archives of General Psychiatry 38 (April 1973): 636-640.

[79] J. Gordon Millichap, ed., Modern Treatment, 6 vols. (New York: Hoeber Publishing Co., 1969), 6:1233-1246.

[80] Benjamin Pasamanick, "Anticonvulsant Drug Therapy of Behavior Problem Children with Abnormal Encephalograms," Archives of Neurology 65 (July 1951):752.

[81] J. Gordon Millichap et al., "Auditory Perceptual Deficit Correlated with EEG Dysrhythmias: Response to Dyphenylhydantoin Sodium" Neurology 19 (September 1969):870-872.

[82] Millichap, "Drugs," p. 329; C. Keith Conners, Psychopathology Disorders of Childhood, eds., John S. Werry and Richard Quay (New York: Eiley and Sons Publishers, 1972):316-347.

dates back to 1937, when Charles Bradley observed that racemic amphetamine produced "spectacular" effects on a number of children displaying disturbed behavior.[83] He wrote:

> 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.[84]

Not only was it apparent to Bradley that a paradoxical calming effect on behavior could be attributed to the drug; he also noted an improvement in the school work of approximately fifty percent of the children.[85] Thus, two distinct avenues of research were opened based on Bradley's initial observations: the paradoxical calming effect of amphetamine on observed behavior and the stimulating effect of the drug on school work.

By 1950, however, after twelve years of observing a total of 388 children treated with amphetamines, Bradley concluded that the effects on these children might not be so paradoxical.[86] Despite this fact, research proceeded on the assumption that the effects of amphetamines on hyperactive children was indeed paradoxical.

If the effect wasn't paradoxical, how then could the improvement in observed behavior be explained? Bradley was not too far away from one of the explanations presently given when he considered the possibility of

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[83]Charles Bradley, "The Behavior of Children Receiving Benzedrine," American Journal of Psychiatry 94 (November 1937):584.

[84]Ibid., p. 582 [85]Ibid.

[86]Charles Bradley, "Benzedrine and Dexedrine in the Treatment of Children's Behavior Disorders," Pediatrics 5 (January 1950):24-37.

stimulation of neural inhibition areas as an explanation for the observed effect. Laufer suggested that amphetamines stimulated the inhibitory functioning of the diencephalon (brain stem), thus cutting off irrelevant stimuli before they reached the cortex.[87] P.B. Bradley demonstrated with cats that the possible site of amphetamine action was the brain stem reticular activating system, the area of the brain responsible for maintaining alertness. An increase in alertness would cause an increase in focused attention and a decrease in response to irrelevant stimuli.[88] Since the reticular activating system is located in the diencephalon both Laufer and Bradley appear to be correct. If the site of amphetamine action is the brain stem, then the drug's stimulating effects would both increase alertness and prevent irrelevant stimuli from reaching the cortex. In either case the behavior of some hyperactive children would appear to improve, not paradoxically, but as a normal result of the stimulating effects of amphetamine.

C. Keith Conners offers another explanation for the apparently paradoxical calming effect of amphetamines. He believes that the subdued behavior might well be an "artifact of observation" reflecting not gross body movement as such but rather the way in which the movement is organized relative to the social demands of the situation.[89] Because the behavior of the hyperactive child was channeled into more acceptable activities s/he

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[87] Laufer, Denhoff, and Solomons, "Hyperkinetic Impulse Disorder," p. 43.

[88] P. B. Bradley, "The Effect of Some Drugs on the Electrical Activity of the Brain of the Conscious Cat," Electroencephalography and Clinical Neurophysiology (August 1953):21; P.B. Bradley and John Elkes, "The Effects of Some Drugs on the Electrical Activity of the Brain," Brain 80 (March 1957):77-117.

[89] C. Keith Conners, "The Effect of Dexedrine on Rapid Discrimination and Motor Control of Hyperkinetic Children Under Mild Stress," Journal of Nervous and Mental Disease 142 (May 1966):432.

appeared to be more subdued.

Whether the effects of amphetamine treatment on behavior were paradoxical or not certainly didn't make much of a difference on the number of improvements reported. Significant improvement in behavior as rated by parents, teachers, and caretakers is the most consistently reported result.

Weiss et al. reported a significant reduction in hyperactivity as perceived by mothers, teachers, and psychologists of thirty-eight children between the ages of six and twelve who had been treated with stimulants.[90] Eisenberg, Conners, and Sharpe indicated that teacher ratings of a group of stimulant-treated children were significantly more favorable than were ratings of a placebo group. The teachers reported improvements in academic performance, classroom behavior, attitude toward authority, attitude to peers, and overall behavior.[91] Conners, Eisenberg, and Barcai reported significant improvement in teacher ratings of behavior of fity-two public school children referred for learning problems and treated with dextroamphetamine.[92] Steinberg, Troskinsky, and Steinberg; Greenberg, Deem, and McMahon; MacKay, Beck, and Taylor; and Schain and Reynard also report improvements in behavior resulting from stimulant treatment.[93] There seems

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[90]George Weiss et al., "Studies on the Hyperactive Child - V: The Effects of Dextroamphetamine and Chlorpromazine on Behavior and Intellectual Functioning," Journal of Child Psychology and Psychiatry 9 (December 1968): 145-156.

[91]Leon Eisenberg, C. Keith Conners, and Lena Sharpe, "A Controlled Study of the Differential Application of Outpatient Psychiatric Treatment for Children," Japanese Journal of Child Psychiatry 6 (Fall 1965):125-134.

[92]C. Keith Conners, Leon Eisenberg, and Alfred Barcai, "Effect of Dextroamphetamine on Children: Studies on Subjects with Learning Disabilites and School Behavior Problems," Archives of General Psychiatry 17 (October 1967):478-485.

[93]Grace G. Steinberg, Charles Troskinsky, and Harry Steinberg, "Dextroamphetamine-Responsive Behavior Disorder in School Children," American Journal of Psychiatry 128 (August 1971):66-71;

to be little doubt about the efficacy of stimulant drugs to improve behavior, at least as rated by parents, teachers, and caretakers.

In more controlled, objective studies utilizing various instruments to measure activity levels, results were more contradictory however. Sprague, Barnes, and Werry found that methylphenidate without regard to dosage level significantly reduced activity level as measured by a stabilmetric cushion. The subjects were twelve emotionally disturbed boys. Placebo was found to have no effect.[94] Millichap et al., however, in a well-controlled study of thirty hyperactive underachievers; found that methylphenidate tended to reduce motor activity, as measured by an actometer (an activity-watch worn on the wrist which measures locomotion on a horizontal plane). Placebo was reported to have a similar effect in this study and diminished the significance of the findings.[95] In another study by Millichap and Boldrey, actometer-measured motor activity was actually increased when subjects were treated with methylphenidate, even though parents and teachers rated the subjects as exhibiting improved motor coordination and reduced impulsivity.[96]

Greenberg, Deem, and McMahon, pp. 44-51; Mary C. MacKay, Leah Beck, and Reginald Taylor, "Methylphenidate for Adolescents with Minimal Brain Dysfunction," New York State Journal of Medicine 73 (February 1973):550-554; Richard J. Schain and Carol L. Reynard, "Observations on Effects of a Central Stimulant Drug (Methylphenidate) in Children with Hyperactive Behavior," Pediatrics 55 (May 1975):709-716.

[94]Robert L. Sprague, Kenneth R. Barnes, and John S. Werry, "Methylphenidate and Thioridazine: Learning, Reaction Time, Activity, and Classroom Behavior in Disturbed Children," American Journal of Ortho-Psychiatry 40 (July 1970):615-628.

[95]J. Gordon Millichap et al., "Hyperkinetic Behavior and Learning Disorders - III: Battery of Neuropsychological Tests in Controlled Trial of Methylphenidate," American Journal of Diseases of Children 116 (September 1968):235-244.

[96]J. Gordon Millichap and Edward E. Boldrey, "Studies in Hyperkinetic Behavior: II. Laboratory and Clinical Evaluations of Drug Treatments," Neurology 17 (May 1967):467-471.

These results seem to indicate that, as Conners stated, the paradoxical calming effect of stimulants on hyperkinetic children may, indeed, be an artifact of observation.[97]

The Conners, Eisenberg, and Barcai study already mentioned offers support to Conners hypothesis. The study involved fifty-two public school children referred for learning and behavior disabilities. Over a one-month period 10 mg of dextroamphetamine was administered daily to each subject. A factor analysis of objective personality and performance tests revealed that dextroamphetamine had no significant effect on a factor representing ability and performance, but did produce a highly significant improvement on a factor representing assertiveness, drive for achievement, and vigor of response. Teachers, however, rated overall performance and behavior as improved.[98]

It will be recalled that in Bradley's 1937 study it was stated that fifty percent of the stimulant-treated children demonstrated improvement in school work.[99] The suggestion being that drug treatment in some way directly facilitated learning. In the same year that Bradley published his original results, two researchers reported findings which suggested that Benzedrine had positive effects on test scores.[100] Further support for the idea that cognitive and intellectual functioning was enhanced by administration of these drugs came from Cutler, Little and Strauss in 1940, and from Bradley and Bowen

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[97] C. Keith Conners, "The Effect of Dexedrine," p. 432.

[98] Conners, Eisenberg, and Barcai, pp. 481-483.

[99] Bradley, "Behavior of Children," p. 582.

[100] Michael Molitch and John P. Sullivan, "The Effect of Benzedrine Sulfate on Children Taking the New Stanford Achievement Test," American Journal of Orthopsychiatry 7 (October 1937):519-522.

in 1941.[101]

However, more recent methodologically sound studies indicate that changes in higher cognitive and intellectual functions may not be a direct effect of the drugs but may rather be a result of "more limited drug-induced changes in specific aspects of the information-processing sequence."[102] More specifically, Eisenberg and Conners pointed out that "there is good reason to suppose that stimulants alter the child's ability to attend to the task at hand; and given such alterations, almost any task will show enhanced performance . . .,"[103] especially if the child has been deficient in a given area to begin with.

It appears that amphetamines work on hyperactive children by stimulating specific inhibiting areas of the brain and allowing them to increase alertness by filtering out irrelevant stimuli. The effects are not paradoxical, and also, the apparent calming effect of stimulants may only be an artifact of observation. Stimulants also do not improve cognition and perception. The fact that hyperactive children appear to perform better academically when under stimulant influence is probably related to the ability of the drug to facilitate attention to specific tasks. This is also probably related to the stimulating effect of the drugs on the inhibitory function of the brain.

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[101] Martin A. Cutler, James W. Little, and Alfred A. Strauss, "The Effect of Benzedrine on Mentally Deficient Children," American Journal of Mental Deficiency 45 (July 1940):59-65; Charles Bradley and Methew Bowen, "Amphetamine (Benzedrine) Therapy of Children's Behavior Disorders," American Journal of Orthopsychiatry 11 (January 1941):92-103.

[102] Leon Eisenberg and C. Keith Conners, "Psychopharmacology in Childhood," in Behavioral Science in Pediatric Medicine, eds., Norman Talbot, Jerome Kagan, and Leon Eisenberg (Philadelphia: W.B. Saunders Publishers, 1971), p. 414.

[103] Ibid., p. 415.

The major stimulant drugs used today to treat hyperactivity are methylphenidate (Ritalin), dextroamphetamine (Dexedrine), pemoline (Cylert), racemic amphetamine (Benzedrine), Denol (Deaner), and levoamphetamine.

According to Goodman and Gillman, methylphenidate "is an important adjunct in the therapy of hyperkinetic syndromes in children . . ."[104] It is also stated that:

> . . . methylphenidate is a mild CNS stimulant with more prominent effects on mental than on motor activities. However, large doses produce signs of generalized CNS stimulation that may lead to convulsions in man and animals. Its pharmacological properties are essentially the same as those of amphetamines. Methylphenidate also shares the abuse potential of the amphetamines.[105]

Methylphenidate is presently the drug of choice for treating hyperactivity in children because it has been reported to have fewer side-effects than other stimulants.[106]

This, however, has seriously been questioned by Winsberg et al. They showed, in trials using methylphenidate and dextroamphetamine with twelve children, that side-effects were generally distributed between both drugs. One case each of methylphenidate-induced dyskinesia and dextroamphetamine-induced toxic psychosis was reported.[107]

The efficacy of methlphenidate and its effect on behavior and learning has been studied extensively and most studies conclude that methylphenidate is effective in improving both in hyperactive children.[108] So effective has

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[104] Goodman and Gilman, p. 365.

[105] Ibid.

[106] Millichap, "Drugs," p. 321; Werry, "Medication," p. 83.

[107] Bertrand Winsberg et al., "Dextroamphetamine and Methylphenidate in the Treatment of Hyperactive/Aggressive Children," Pediatrics 53 (April 1974):236-241.

[108] Steinberg, Toskinsky, and Steinberg, p. 70; Greenberg, Deem, and McMahon, p. 49; Schain and Reynard, p. 714.

methylphenidate proven itself to be, that it is presently used as a standard against which new drugs are compared.[109]

As with all stimulants, caution regarding the dosage of methylphenidate should be exercised. A report of the Council on Health states that 2mg/kg per day is recommended. This represents a dose of up to 80 mg methylphenidate per day in larger children.[110] However, more systematic studies of dosage suggest that children respond at a level as low as 0.3mg/kg methylphenidate or 10 to 15mg daily for an average child.[111] This is important since it has been shown that high doses of methylphenidate may cause anorexia, weight loss and suppression of growth. The "high" doses start at 20 mg per day.[112] It has been suggested that the suppression of growth is a temporary condition evident only at the beginning of drug treatment, but Safer, Allen and Barr have shown that the condition exists as long as medication is given, but doesn't occur until the dose of methylphenidate exceeds 20mg per day.[113]

The first stimulants used in the treatment of hyperactivity were the amphetamines, racemic amphetamine (Benzedrine) and dextroamphetamine (Dexedrine).[114] More recently, several researchers have indicated a preference for levoamphetamine succinate (Cybil), at one time considered an inert

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[109] Werry, "Medication," p. 83.

[110] Council on Child Health, "Medication for Hyperkinetic Children," Pediatrics 55 (April 1975):560-561.

[111] Robert L. Sprague and Esther Sleator, "What is the Proper Dosage of Stimulant Drugs in Children?" International Journal of Mental Health 4 (January 1975):75-104.

[112] Daniel Safer, Richard Allen, and Evelyn Barr, "Depression of Growth in Hyperactive Children on Stimulant Drugs," New England Journal of Medicine 287 (July 1972):217-220.

[113] Ibid., p. 217.

[114] Bradley, "Benzedrine and Dexedrine," pp. 24-37.

contaminant of racemic amphetamine.[115] This preference is based on three major studies utilizing children and dogs.

Arnold et al. found that when dosages of dextroamphetamine and levoamphetamine were kept equal both drugs produced effects that were significantly greater than placebo. Statistical measurement based on a teacher's symptom checklist, parent's symptom checklist, pulse, blood pressure, weight, and parental quantification of previously identified target symptoms showed that levoamphetamine appeared as potent as dextroamphetamine. The researchers concluded that levoamphetamine might be useful for some children.[116]

Corson et al. found that levoamphetamine, in the same doses as dextroamphetamine, was beneficial in treating a hostile and aggressive dog, but was not as good as dextroamphetamine in treating dogs who were not aggressive but merely nervous and hyperactive. These researchers concluded that "a clinical distinction might be fruitful between the hostile-aggressive and the overactive-'nervous' manifestations of the hyperkinetic syndrome."[117]

The third study based on diagnostic criteria, defined by Fish,[118] indicated that levoamphetamine was statistically equal to dextroamphetamine (both being significantly better than placebo) in treating "unsocialized-

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[115]L. Eugene Arnold and Paul H. Wender, "Levoamphetamine's Changing Place in the Treatment of Children with Behavior Disorders," Clinical Use Stimulant Drugs in Children, ed. C. Keith Conners (New York: American Elsevier Publishing Co., Inc., 1974,) p. 179.

[116]L. Eugene Arnold et al., "Levoamphetamine and Dextroamphetamine: Comparative Efficacy in the Hyperkinetic Syndrome," Archives of General Psychiatry 27 (July 1972):816.

[117]Samuel A. Corson et al., "Tranquilizing Effects of d-Amphetamine on Hyperkinetic Untrainable Dogs," reported in Arnold & Wender, p. 182-183.

[118]Barbara Fish, "The 'One Child, One Drug' Myth of Stimulants in Hyperkinesis," Archives of General Psychiatry 25 (September 1971):193-203.

aggressive" hyperactive children. By contrast in the "overanxious-hyperkinetic" group, levoamphetamine was shown to be no better than placebo, while dextroamphetamine was significantly better than both. Ratings of parents, teachers, and psychiatrists were used in both cases.[119]

Next to methylphenidate, the drugs of choice for treating hyperactive behavior in children are dextroamphetamine and racemic amphetamine. Goodman and Gilman report that these amphetamine drugs are powerful central nervous system stimulants with a high degree of abuse potential.[120] Interestingly, Goodman and Gilman state that:

> The central stimulant effects of amphetamine were first used clinically in 1935 to treat narcolepsy and have since been employed in a variety of conditions, including obesity, fatigue, parkinsonism, and poisoning by CNS depressants.[121]

No mention is made of their use in the treatment of hyperactivity. Nevertheless they have been used extensively, since Bradley's 1937 study, to treat hyperactive behavior.

Millichap, in summarizing the use of amphetamines in several studies of hyperactivity since Bradley, states that of 610 patients treated, improvement in behavior occurred in an average of sixty-nine percent and that hyperactivity was made worse in eleven percent.[122] The volume of literature relating the effects of amphetamines on hyperactivity is immense. A bibliography of these studies would consititute a rather lengthy report of its own. Amphetamine effect has been studied in connection with arousal

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[119] L. Eugene Arnold et al., "Levoamphetamine and Dextroamphetamine: Differential Effect on Aggression and Hyperkinesis in Children and Dogs," American Journal of Psychiatry 130 (February 1973):165.

[120] Goodman and Gilman, pp. 496-498.

[121] Ibid., p. 496.

[122] Millichap, "Drugs," p. 325.

responses to the reticular activating system; rapid discrimination and motor control of hyperkinetic children; perception, learning, and achievement; behavior and performance of hyperactive children; reaction time and activity; and attention in hyperactive children.[123] One study even suggests its use in the "treatment" of juvenile delinquency.[124]

This widespread use of amphetamine to treat hyperactivity has been highly criticised. Most of the criticism in the literature stems from two areas: the abuse potential of amphetamines and the side-effects of amphetamines. The abuse potential of amphetamines was, until 1972, usually regarded as a cautious supposition in many studies and as a scare tactic utilized by critics of drugging children.[125] However, in long term studies, some of twenty years duration, no evidence of patient abuse of drugs has been found.[126] Particular caution has been suggested since a strong familial tendency towards alcoholism in families of hyperactive children has been shown.[127]

Possible side-effects of amphetamines reported by Goodman and Gilman include headache, palpitation, dizziness, vasomotor disturbances, agitation,

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[123]Lester Grinspoon and Susan B. Singer, "Amphetamines in the Treatment of Hyperkinetic Children," Harvard Educational Review 43 (Winter 1973): 515-555.

[124]Barry M. Maletzky, "d-Amphetamine and Delinquency: Hyperkinesis Persisting," Diseases of the Nervous System 35 (December 1974):543-547.

[125]Carole W. Ofir, "A Stavish Reliance on Drugs: Are We Pushers for Our Own Children?" Psychology Today (December 1974):49.

[126]Leon Eisenberg, "Symposium: Behavior Modification by Drugs: III. The Clinical Use of Stimulant Drugs in Children," Pediatrics 49 (May 1972): 709-715; George Weiss, "The Natural History of Hyperactivity in Childhood and Treatment with Stimulant Medication at Different Stages: A Summary of Research Findings," International Journal of Mental Health 4 (February 1975): 213-226.

[127]Dennis P. Cantwell, "Psychiatric Illness in the Families of Hyperactive Children," Archives of General Psychiatry 27 (March 1972): 414-417.

confusion, dysphoria, apprehension, delirium, or fatigue. They also state of amphetamines that:

> All are capable of producing generalized convulsions in sufficient doses. Unfortunately, the margin of safety of doses . . . is generally very narrow and unpredictable. No totally safe . . . stimulant is currently available.[128]

Also, toxic doses are said to be idiosyncratic after as little as 2 mg but are rare with doses of less than 15 mg.[129]

In one study, dextroamphetamine was associated with "significant personality deterioration" in twenty percent of the population treated. The authors recommended extreme care be taken to assess the underlying personality organization of patients before administering the drug.[130] Methylphenidate, whose pharmacological properties are very similar to amphetamine, has also been implicated in causing such disturbances.[131]

Presently, most of the criticism concerning side-effects of amphetamines has been generated from the report of Safer and Allen that these drugs can cause a permanent suppression of growth in many children. They indicated that a "mean yearly weight gain of nine children on medication for two years was 1.8kg as compared to the expected gain of 3.1kg." Depression of growth in height was more variable, but children whose weight growth was suppressed also evidenced a proportional depression of growth in height. This suppression of growth was seen to occur in children receiving 10-15mg of

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[128] Goodman and Gilman, p. 359.

[129] Ibid., p. 499.

[130] Lawrence M. Greenberg, Shirley A. McMahon, and Michael A. Deem, "Side Effects of Dextroamphetamine Therapy of Hyperactive Children," Western Journal of Medicine 120 (February 1974):105-109.

[131] Philip Ney, "Psychosis in a Child Associated with Amphetamine Administration," Canadian Medical Association Journal 97 (October 1967): 1026-1029.

amphetamine per day.[132] This certainly merits much consideration since the Council on Child Health indicates that acceptable daily doses of dextroamphetamine may be as high as 40mg.[133] In a later study, the authors found that discontinuance of the drugs "resulted in a growth rebound . . . which was 15 - 68% above the age-expected increment."[134]

The effects of two other stimulants, deanol and pemoline, have recently been studied in connection with hyperactivity. Lewis and Young reported that both deanol and methylphenidate appeared to improve performance in children with behavior disorders, but the mechanism of action attributed to deanol remains speculative. They indicate that further clinical studies on deanol are necessary to more fully assess its effect on hyperactive children.[135]

Pemoline (Cylert) is a central nervous system stimulant that has recently been approved by the U.S. Food and Drug Administration for treatment of "minimal brain dysfunction in children over six." It is reported to be chemically different from either methylphenidate or amphetamines and can be given in single daily doses. (Methylphenidate and amphetamine are usually prescribed to be taken twice daily.) The drug has been previously tried in the treatment of senility, anxiety, depression, and schizophrenia.[136]

Conners reported that pemoline "may have more effects on selective attention than dextroamphetamine, but both drugs act to increase cortical

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[132] Safer, Allen, and Barr, "Depression of Growth," p. 217.

[133] Council on Child Health, p. 560.

[134] Daniel J. Safer, Richard P. Allen, and Evelyn Barr, "Growth Rebound After Termination of Stimulant Drugs," Journal of Pediatrics 86 (January 1975):113.

[135] James A. Lewis and Rosemarie Young, "Deanol and Methylphenidate in Minimal Brain Dysfunction," Clinical Pharmacology and Therapeutics 17 (January 1975):534-540.

[136] The Medical Letter 18 (January 1976):5-6.

arousal."[137] More specifically it was found that pemoline may augment information processing when visual discrimination is required, but may reduce attention to visual stimuli when they are irrelevant to a particular task.[138] Dykman, McGrew, and Ackerman report that pemoline improves attention and decreases the level of restlessness in hyperactive children. Improvement in performance was noted in reading and arithmetic, auditory perception, motor coordination involving complex left-right maneuvers, and attention to details and organization.[139] Page et al., in two studies, indicates that improved performance in gross behavior, cognition, and perception are achieved with minimal side-effects in a once-daily regimen of pemoline. They recommend that pemoline may be a "highly useful" alternative to amphetamines and methylphenidate as an adjunct in the management of hyperactivity.[140]

The most common adverse side-effects of pemoline, as with other central nervous stimulants, are insomnia and anorexia. Other adverse effects include abdominal pain, restlessness, and palpitations. It has also been recommended, since suppression of growth has been determined as an adverse effect of

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[137] C. Keith Conners, "The Effect of Pemoline and Dextroamphetamine on Evoked Potentials Under Two Conditions of Attention," Clinical Use of Stimulant Drugs, ed., C. Keith Conners (New York: American Elsevier Publishing Co., Inc., 1974) p. 137.

[138] Ibid., p. 135.

[139] Roscoe Dykman, Jeanette McGrew, and Peggy T. Ackerman, "A Double-Blind Clinical Study of Pemoline in MBD Children: Comments on the Psychological Test Results," Clinical Use of Stimulant Drugs, ed., C. Keith Conners (New York: American Elsevier Publishing Co., Inc., 1974):127.

[140] John G. Page et al., "A Multi-Clinic Trial of Pemoline in Childhood Hyperkinesis," Clinical Use of Stimulant Drugs in Children, ed., C. Keith Conners (New York: American Elsevier Publishing Co., Inc. 1974): 98-124; John G. Page et al., "Pemoline (Cylert) in the Treatment of Childhood Hyperkinesis," Journal of Learning Disabilities 7 (October 1974): 42-47.

other stimulants, that careful monitoring of height and weight be maintained for children receiving pemoline.[141]

The Controversy

The confusion apparent in the medical community in describing hyperactivity, and the danger involved in prescribing behavior-modifying drugs for its treatment, has led to much controversy among professionals concerned with the welfare of the children involved. This controversy has basically centered on the studies which have purported the efficacy and safety of the drugs used, the numbers of children involved, and the social implications of controlling children's behavior with drugs.[142]

Grinspoon and Singer have criticized the studies espousing the positive effects of drugs and their reported usefulness in treating hyperactivity. They stated that although experimental drug administration had been well-controlled, many variables were uncontrolled. It is also indicated that subject populations in many studies were heterogeneous in their diagnosis, reasons for referral, and types of learning difficulties. Even in the studies that dealt specifically with hyperactivity there was no general agreement on criteria for selection. Finally, the authors state that the studies were not comparable on rating instruments and measurements used. They conclude that, "although statistically significant findings abound it is difficult to assess their meaning."[143]

Among researchers who have studied the behavior-modifying drugs and their effects on children, there appears to be a consensus that these drugs are being overprescribed and overly relied upon in treating hyperactivity.

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[141] Medical Letter, p. 6.

[142] Divoky and Schrag, pp. 69-107.

[143] Grinspoon and Singer, pp. 524-525.

Sprague and Sleator:

> . . . feel strongly that psychotropic drugs have all too frequently been prescribed and used without proper consideration of the viewpoints and information from the school system, the parents, and the child.[144]

Gerald Solomons states:

> . . . that drugs for minimal brain dysfunction are not being properly employed by many of us.[145]

Leon Eisenberg:

> Drugs promise neither the passport to a brave new world nor the gateway to the inferno. Properly employed as a single component of a total treatment program they can be helpful in realizing the goal of the healthy development of children.[146]

Weithorn and Ross ask, "who is being medicated?" They state that many of the behavioral studies on which the clinical use of medication is based, involved subjects whose disturbances were severe enough to warrant referral and in many cases, institutionalization.[147] In recent years there has been a marked increase in the number of children considered to be hyperactive.[148] While it is possible that this number has risen, it is probably more accurate to assume, based on the subjective nature of defining the problem, that children who in earlier years might have been placed in

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[144]Robert L. Sprague and Esther K. Sleator, "Effects of Psychopharmacologic Agents on Learning Disorders," Pediatric Clinics of North America 20, ed., Herbert Grossmann (Philadelphia: W.B. Saunders Company, 1973):719.

[145]Gerald Solomons, "Drug Therapy: Initiation and Follow-up," Annals of New York Academy of Sciences 205 (February 1973):343.

[146]Leon Eisenberg, "Symposium: Behavior Modification by Drugs III. The Clinical Use of Stimulant Drugs in Children," Pediatrics 49 (May 1972): 713.

[147]Corinne J. Weithorn and Roslyn Ross, "Stimulant Drugs for Hyperactivity: Some Additional Disturbing Questions," American Journal of Orthopsychiatry 46 (January 1976):169-171.

[148]Divoky and Schrag, pp. xi-xvii.

another diagnostic category (emotionally disturbed, antisocial, etc.) are now being labelled hyperactive or MBD or one of the other numerous labels. Most of these children are subsequently being drugged. Also, the expectation that drugs will be prescribed and will alter undesirable behavior may be influencing the referral process. "It is quite possible that many of the children who are receiving drugs today are far less in need of medical treatment than those on whom the original successes were established."[149]

Other criticism has been directed at assessment procedures in determing if a child's functioning warrants drugs. What is "too much activity," or "too little concentration?" What is the range of allowable behavior in young children? Who's to make the judgement? Usually it's not the physician whose medical examination pinpoints the problem or even the complaints of children themselves that imply the need for drugs. All too often the child is reported, by teachers or parents, to be failing in the complex demands of his social situation.[150] Weithorn and Ross state that:

> This . . . situation may include a number of variables intervening between observed hyperactivity and possible dysfunctioning of the central nerous system. Among these are the child-teacher ratio in the classroom, the frustration tolerance of the teacher or parent, the type and appropriateness of the instructional materials, the degree of disorganization in the child's home life, emotional stress, inadequacy of nutrition and diet, or boredom . . .[151]

Conners and Rothschild, echoing this criticism, state:

> What we actually observe is not a deficit in the process of learning but rather a failure of the child in the complex

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[149]Weithorn and Ross, p. 170.

[150]Ellen Bowman Welsch, "You May Not Know It, but Your Schools Probably are Deeply into the Potentially Dangerous Business of Teaching with Drugs," American School Board Journal 161 (February 1974):41-45; Diane H. Browning, "Before Giving Drugs for Hyperkinesis," Drug Therapy (September 1975): 42-53.

[151]Weithorn and Ross, p. 170.

> social matrix of the school world. Failure, therefore, is partially a social value judgement and not a statement of fact.[152]

One cannot help but ask at this point why it is that the children need drugging when the social system in which they are living is not functioning. Some critics feel that the decision to drug is one rooted in the politics of control and submission to authority.[153] Diane Divoky and Peter Schrag, the most recent and eloquent critics of present educational and medical policies, believe that it is inconsistent "that while the government is throwing people in jail for using speed, other governmental institutions are pushing it on school children."[154] They go on to state:

> It is the ideology of drugging, the idea that people can and should be chemically managed, that represents the most pervasive imposition on liberty and the most dangerous extension of authority. The seductive counterargument that a certain drug isn't hurting a certain child . . . and that one should not sacrifice his well-being to some political abstraction, is itself a disguised political argument in defense of the standards that determine his "happiness" and success. The argument seems to prove that while the child may not become dependent on the drug, those who recommend and defend it already are.[155]

One other point stressed by Divoky and Schrag is that the FDA no longer considers minimal brain dysfunction a sufficient cause to warrant drug prescription. But the drugs would be prescribed to treat short attention span, impulsivity, lack of concentration or any of a number of behavioral elements. This was done in the light of a great number of studies

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[152] C. Keith Conners and G. Rothschild, "Drugs and Learning in Children," in Learning Disabilities, vol. 3, ed., J. Helmuth (Seattle: Special Child Publications, 1968), p. 199.

[153] Divoky and Schrag, p. 87; Charles Witter, "Drugging and Schooling," Trans-Action: Social Science and Modern Society 8 (July/August 1971):31-34.

[154] Divoky and Schrag, pp. 106-107.

[155] Ibid., p. 106.

which were unable to successfully define or diagnose hyperactivity. The objections about the lack of a definable syndrome had been removed. "The drugs were placed openly, officially and legally into the realm of behavior control."[156]

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[156]Divoky and Schrag, p. 107.

CHAPTER III

DISCUSSION

It is apparent that the controversy inherent in modifying childrens' behavior with chemical agents is not readily amenable to solution. However, several avenues of relief should be investigated.

1) Physicians must re-evaluate the concept of drug abuse. Even though there is no indication in follow-up studies of individual abuse of drugs by children, there certainly appears to be mounting evidence of collective abuse of drug prescribing habits by physicians.

2) The fact that drugs, especially the stimulants, have been shown to suppress growth in children can be expanded to include psychological as well as physiological growth. Dr. Mark Steward has said of drug-treated children:

> They come off drugs at fourteen or so and suddenly they're big strong people who've never had to spend any time building any controls in learning how to cope with their own daily stress. Then the parents, who have forgotten what the child's real personality was like without the mask of the drug, panic and say, "Help me, I don't know what to do with him. He's taller than I am and he has the self-discipline of a six year old."[1]

3) Those involved in the diagnosis of hyperactive children, especially pediatricians, must pay closer attention to their assessment procedures. Studies have shown that there may, indeed, be a hyperactive child who might benefit from medication, but not in the numbers presently being treated.[2]

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[1] Divoky and Schrag, p. 87.

[2] Martin Bax, "The Active and the Over-Active School Child," Developmental Medicine and Child Neurology 14 (January 1972):83-86.

Certainly the numerous possible etiologies suggested should be assessed before a drug regimen is begun.

4) The need for interdisciplinary communication is paramount. No member of any profession involved in the assessment, treatment, or remediation of the hyperactive child should function without the active participation of members of related disciplines, parents, and the children themselves. Drug treatment should be considered an adjunct to treatment of the hyperactive child. It should not be accepted as a panacea. Too often, it seems that once the children are sedated and seated they are forgotten. It behooves the prescribing pediatrician, in this day of medical malpractice pay-offs, to make sure that the drugs s/he prescribes are being used in the suggested manner: as an adjunct in total treatment.

5) The problems of terminology and classification and definition of the hyperactive child as a medical entity appear, at this point, to be beyond solution. For this reason, it is suggested that the symptoms of hyperactivity be considered in a psychoeducational context. Medical definitions lead to conclusions about cerebral status and remote etiology which usually have little direct relevance to what the teacher or parent is trying to do in academic or behavioral training.

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