Commentary with a Historical Perspective by a Child Psychiatrist: When “ADHD” Was the “Brain-Damaged Child”

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ONCE UPON A TIME, when I graduated from medical school (in 1946, to be precise about it), there was no attention-deficit/hyperactivity (ADHD); that is, there was no such term. There were, of course, children with a similar constellation of symptoms (though there seemed to be many fewer), but they were categorized by different labels reflecting different concepts. One term in common use was “the brain-damaged child.” In a paper I wrote on such children (Eisenberg 1957), I summarized the prominent clinical features: hyperkinesia; short attention span and marked distractibility; lability of mood; anxiety, sometimes reaching the proportions of panic; a greater or lesser degree of intellectual deficit; and, less consistently, antisocial behavior.

Where did the concept of “the brain-damaged child” (or minimal brain damage or minimal brain dysfunction, all in use in the 1950s and 1960s) come from? Bond and Smith (1935) had described such symptoms in children who had survived an episode of encephalitis and proposed “post-encephalitic syndrome” as the diagnosis. The use of the term *brain-damaged* (in the absence of overt neurological signs or history of known neurological disease) originated with Strauss and Werner (1942). Brain damage was inferred from behavioral symptoms; it was not validated by independent data. Attaching the widely used adjective “minimal” to the

phrase (Pasamanick and Knobloch 1959; Walzer and Wolff 1973) did not increase its accuracy or its scientific validity (Birch 1964).

Some of us were uneasy with a diagnosis implying that (1) the clinical problems were secondary to tissue damage (in the absence of direct evidence of tissue damage) and (2) injuries anywhere in the brain would produce a common phenotype (Eisenberg 1957; Birch 1964; Klein and Gittelman-Klein 1974). Given just how unsatisfactory the term was, why did it persist? It served as a rallying point for those of us who insisted that the brain mattered for behavior in a day when psychogenesis ruled the roost (Eisenberg 1960), that is, when psychiatry was “brainless” (Eisenberg 1986). In many public school jurisdictions, the diagnosis led to additional services for such children because of the implication that their problems were organic or endogenous, as opposed to psychological or psychogenic. For this very reason, parents welcomed it. Furthermore, the term *proved* they were not responsible for their child’s problems (no small victory at a time when parent blaming was widespread in child psychiatry and education). With time, the brain-damaged child morphed into “hyperkinetic and inattentive” child and finally into ADHD.

The first edition of the APA *Diagnostic and Statistical Manual of Mental Disorders* (DSM I),

published in 1952, did not include the hyperkinetic syndrome. Mike Rutter and I participated in a World Health Organization Seminar on Diagnosis and Classification in Child Psychiatry in 1967. We had to argue vigorously for the inclusion of hyperkinesis as a syndrome (Rutter et al 1969). Other participants were highly skeptical about the frequency with which the diagnosis of hyperkinesis was used in the United States. Most U.K. psychiatrists allocated the symptom complex to the category 'behavior disorder'. We won the debate. In consequence, hyperkinetic reaction of childhood appeared as a category in DSM II in 1968. It was not, however, until DSM III (1980) that attention-deficit/hyperactivity disorder (ADHD) entered the official lexicon.

Whatever the controversies about its terminology and its pathophysiology, it was the only syndrome in child psychiatry for which there was a widely agreed on medication: *d*,1-amphetamine, first identified by Charles Bradley in 1937. Shortly after the new drug came on the market, Bradley tried it out on a diverse group of child psychiatric inpatients. An astute clinician, he recognized the unexpected. Though the drug (or its stronger isomer, dextroamphetamine) was classified pharmacologically as a stimulant, it calmed overactive children on the ward and had little effect on the others (Bradley 1937). The third edition of Leo Kanner's *Child Psychiatry* (1957) included a 3-page chapter on pharmacological adjuvants used for treatment (the size of the chapter reflected the status of pharmacotherapy in the 1950s). Dextroamphetamine was the *only* drug listed as effective. However, like all medical and psychiatric treatments of that period, it had never been put to an exacting test of efficacy. This should hardly be surprising in view of the fact that the first double-blind randomized trial (RCT) in all of medicine (a trial of streptomycin for tuberculosis) did not take place until 1948 (Medical Research Council 1948). I was the principal investigator on the first National Institute for Mental Health (NIMH) grant for child psychopharmacology RCTs (Lipman 1974). Our research group demonstrated the efficacy of dextroamphetamine (Eisenberg et al.; Conners et al. 1967) and later of methylphenidate

(Eisenberg 1971), findings repeatedly confirmed since that time.

What none of us anticipated was the explosion in the diagnosis and treatment of what became ADHD (Batoosingh 1995; Morrow et al. 1998; Zito et al. 1999; Olfson et al. 2003; Centers for Disease Control and Prevention (CDC) 2005). Methylphenidate consumption in "defined daily doses" rose from 60 million in 1987 to 360 million in 1999; prescriptions for methylphenidate, from 4 million to 11 million; and for amphetamines from 1.3 million to about 6 million from 1991 to 1999 (Hearing 2000).

It is, of course, not possible to find data on rates before a given disease has entered the official nomenclature. There are no population-based data on the prevalence of hyperkinetic behavior disorder (or brain-damaged children) for the 1950s and 1960s. At the Conference on Clinical Use of Stimulant Drugs in Children sponsored by the Psychopharmacology Research Center in 1972 (Conners 1974), Jonathan Cole noted how little discussion there had been about "the use of specific drugs in specific psychiatric disorders of childhood" and that "there was essentially no research . . . except for relatively informal work . . ." in a predecessor conference 13 years earlier (Fisher 1959). Ron Lipman commented that, before 1960, interest in the stimulant drug treatment of hyperactive children "was far from overwhelming."

The Isle of Wight study (Rutter et al. 1970) was the first methodologically sound study in child epidemiology. Based on the total population of 2199 ten- and eleven-year-old children with homes on the island, 118 were identified with psychiatric disorder, a rate of 5.4%. No more than 2 of those children were diagnosed with hyperkinetic syndrome, "although a much larger number showed restlessness or over-activity as part of a conduct or neurotic disorder" (p. 201) and "several such children may be included in the antisocial group" (p. 198).

The Centers for Disease Control (2005) has estimated in 2003 an ADHD population prevalence (based on parental reports from the National Survey of Children's Health) at about 4.4 million U.S. children 4–17 years of age. More than 50% of those with the diagnosis (2.5 mil-

lion) were reported to be taking medication for the disorder. The survey reports a remarkably wide difference in the percentage of children with ADHD by state, from about 5.1% in Colorado to 11.2% in Alabama, with an overall U.S. average of about 7.8%. Can such disparities possibly be valid? Are there localized "epidemics" of ADHD or are there "epidemics" of diagnosis? Do the disparities among states reflect differences in the availability of specialists, in fashions in diagnosis, and in their administrative consequences in particular communities or in actual prevalence?

It is useful to recall, in this connection, Judith Rapoport's studies in the late 1970s. Because hyperkinetic children became less active when they took what were by definition stimulant drugs, as though they were taking sedatives, their response was characterized as "paradoxical." When Judy (alone of all of us with the insight and the courage to do it!) put the matter to empirical test by giving a single dose of dextroamphetamine to both normal and hyperactive children and to normal college-aged men, *all* groups showed decreased motor activity, increased vigilance, and improved performance on a learning task. However, the adults reported euphoria, whereas the children reported feeling "tired" or simply "different" (Rapoport et al. 1978; Rapoport et al. 1980). The "paradox" was age related, not disease related. This lesson continues to escape many today. A therapeutic response to stimulant drugs is taken as confirmation of the diagnosis of ADHD. Have we converted a dimensional spectrum that covers the entire population arbitrarily into a diagnosis by imprecise cutoff values? Have child psychiatrists and pediatricians become carpenters with hammers who see all problems as nails?

That such is indeed the case is indicated by the careful epidemiologic research of Angold et al. (2000) and Costello et al. (2003) in rural North Carolina. They report an overall prevalence of unequivocal ADHD among 9–16-year-olds as 0.9%, peaking at 2.2% among 9–10-year-olds and declining to 0.3% at 16. The rate of stimulant treatment was twice the rate of unequivocal ADHD; the majority of stimulant-treated children did not meet criteria for ADHD. They comment that "these results

present a troubling picture of a serious mismatch between need for stimulant treatment and the provision of such treatment."

Claims appeared periodically in the public media in the 1970s that stimulants were being employed as "chemical straightjackets" to suppress minority children (Hearing 1970). All that was missing were empirical data to support the claims! The truth is that African-American children, who receive less medical care for almost all conditions, also receive less psychiatric care, including the prescription of stimulant drugs (Safer and Krager 1992). Minority students in the public schools of Maryland are half as likely to receive treatment with methylphenidate as are white children (Safer and Malever 2000). This remains true whether the child population studied is on Medicaid (Zito et al. 1998) or covered by commercial insurance (Cox et al. 2003).

Social control of the potential for abuse of stimulant drugs has proved difficult to attain. These drugs are useful in the treatment of pathological states, such as narcolepsy and the hyperkinetic syndromes, and for relieving acute fatigue in persons who must meet emergency situations (Laties and Weiss 1962). From the pharmacologic point of view, the more powerful the drug, the greater its potential for untoward side effects. Its virtue is its vice: its very ability to alter fundamental physiological processes. There is no pharmacologic free lunch. The key question is always this: Is the gain to public health from proper use of an agent (taking into account both the extent of benefit to individuals and the number of such individuals in the population) greater than the danger of wide-scale misuse or the social cost of the regulatory machinery itself? Controversies about the best way to control the abuse of stimulant drugs is beyond the scope of this brief article. Contrasting views are evident in Pickering and Stimson (1994) and United Nations Office on Drugs and Crime (2003).

Psychotropic drugs have become a multibillion dollar market. Sponsorship of research by drug companies is pervasive in academia (Studdert et al. 2004). Systematic bias is apparent when companies sponsor research on their own products. Company-sponsored studies are more than 4 times more likely to have outcomes favoring the sponsor than are studies

with neutral sponsorship (Lexchin et al. 2003; Als-Nielsen et al. 2003). Even industry-sponsored meta-analyses are of inferior quality to Cochrane meta-analyses of the same drugs (Jorgenson et al. 2006). Favorable studies are likely to be published multiple times with reports slanted toward commercial advantages (Melander et al. 2003). Unfavorable studies often have not seen the light of day. Leading medical journals now require that therapeutic trials be registered in advance if they wish to be considered for publication when they are completed (DeAngelis et al. 2004).

SUMMARY

ADHD has morphed from a relatively uncommon condition 40 years ago to one whose current prevalence is estimated to be just under 8% of U.S. children 4–17 years of age. Correspondingly, the prescription of stimulant drugs has gone up enormously. The reasons are not self-evident. Is treatment putting misdiagnosed children at risk? Has there been a real change in prevalence? And if so, why? Or are children who were previously missed now coming into care for the first time? These are important questions and warrant systematic investigation. It is time for the NIMH and the FDA to convene senior investigators, clinicians, and epidemiologists to plan large-scale systematic research on matters of serious consequence for child health in America.

DISCLOSURE

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