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Chapter 12

Evolution of a Disorder and Insights into Prevention of ADHD

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Additional information is available at the end of the chapter

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Abstract

Understanding the history of the development of diagnostic criteria for ADHD, the parallel growth of the ADHD drug market, and factors that improve the symptoms of ADHD provides insight into alternative approaches to treatment and the potential for prevention. This chapter sheds light on the rise of ADHD as a diagnostic disorder, and highlights the growth of the ADHD drug market and associated drug sales. The chapter concludes by exploring the potential strategies for preventing ADHD, reviewing research on sleep, omega-3 supplementation, and meditation.

Keywords: ADHD, Executive Function, Meditation, Prevention, Transcendental Meditati

1. Introduction

ADHD is considered the most common chronic disorder of childhood. In the USA, 11% of children aged 4–17 have been diagnosed with ADHD, a 16% increase since 2007 [1]. Some studies suggest that this is a significant underestimation, because the diagnosis may be missed in as many as 50% to 75% of girls (girls often do not exhibit the more disruptive behaviors associated with the disorder). In comparison, all cancers combined affect less than 4% of the population. From this perspective, ADHD might be considered an epidemic among today's children.

Why is it that today greater than 1 in 10 children have ADHD? Where did it come from? When did it appear? What are the possible causes? To gain perspective on the current prevalence of

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ADHD, it is useful to follow the history of the disorder. This can also provide insight into the possibilities for prevention.

2. Origins of drug treatment for ADHD

The first documentation of a disorder relating to impulsiveness in children was in Britain in 1902. Dr. George Still suggested that overactivity and defiant behavior was a "defect of moral control" caused by a genetic tendency toward moral deviation, or the result of an injury at birth. Later, in the 1920s, child survivors of the 1917–1926 pandemic of encephalitis exhibited symptoms of severe behavioral disturbances including hyperactivity. Their behaviors were termed "post-encephalitic behavior disorder".

Drug treatment to control behavior and improve attention emerged when in 1937, Dr. Charles Bradley postulated that amphetamines might help calm children who were in a treatment center for behavioral and neurological problems. Dr. Bradley accidently discovered that children taking the drug also happened to do better in school.

The turning point was in the late 1950s when Dr. Leon Eisenberg conducted the first randomized controlled study of the use of Ritalin for children with hyperactivity. He found the drug to be effective, and therefore concluded the children's behavior was a result of impaired brain functioning, coining the phrase "minimal brain dysfunction" to explain the symptoms. This "dysfunction" was then defined as a mental illness in the Diagnostic and Statistical Manual of Mental Disorders (DSM). The DSM, published by the American Psychiatric Association, covers all mental health disorders of children and adults. The book is considered the "bible" of psychiatric diagnoses. Once a condition is labeled and listed in the DSM, it has credibility and legitimacy as a mental disorder.

In 1961, soon after Dr. Eisenberg's results were published, Ritalin was approved by the FDA for use with children. Ten years later, 150, 000 children were taking the drug. There was, however, no actual scientific evidence underlying the assumption that hyperactivity was the result of brain dysfunction. Consequently, in 1979 the FDA ordered that "minimal brain dysfunction" be eliminated as a diagnostic term.

Around this time, psychiatry was moving from the view that behavior problems are the result of environment (home life and parenting) to the belief that the problems are the result of chemical imbalances. Though, again, there was no scientific foundation for this shift in thinking. The growing availability and use of drug treatment was serving as de facto evidence that the problems must be chemically based since they could be treated, with some effect, by chemicals.

3. Initial concerns about drug treatment

By 1980 the description of hyperactivity in the DSM had morphed into ADHD, with a broadening symptom list. It was beginning to encompass what might previously have been

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accepted as common differences in how children behave. By this time, 500, 000 children were taking Ritalin. Parents were told the drug was mild, safe, and effective.

The active ingredient in Ritalin and most other ADHD medications is methylphenidate, which is an amphetamine. The US government classifies these drugs as Schedule II drugs. Schedule II drugs, which include opiates, are defined as having high potential for abuse, and may lead to severe psychological or physical dependence. ADHD drugs are in the same drug classification as opium, cocaine, morphine, and oxycodone.

From 1990 to 1997, the use of Ritalin increased 700%. In 1996, the US Drug Enforcement Agency (DEA) convened a national conference of experts in research, medicine, public health, and law enforcement to examine the use of the drug with school-age children for the treatment of ADHD. The DEA enforces laws and regulations pertaining to controlled substances. The agency was alarmed by the tremendous increase in the use of Ritalin (the only ADHD drug on the market at the time), and concerned about the dangers of the drug as a Schedule II substance.

Below is an excerpt from comments made by Gene R. Haislip, Deputy Assistant Administrator of the DEA's Office of Diversion Control, at the conclusion of the conference.

> "...there is also strong evidence that the drugs have been greatly over-prescribed in some parts of the country as a panacea for behavior problems. These drugs have been over-promoted, over-marketed and over-sold, resulting in profits of some $450 million annually. This constitutes a potential health threat to many children and has also created a new source of drug abuse and illicit traffic. The data shows that there has been a 1, 000 percent increase in drug abuse injury reports involving methylphenidate for children in the 10 to 14 age group. This now equals or exceeds reports for the same age group involving cocaine. The reported numbers are still small but experts feel that this is only the "tip of the iceberg. "[2]

Though 20 years later there is continued debate as to whether ADHD medication is overprescribed, the issues raised by the DEA remain, as the number of prescriptions for these drugs rise every year.

4. MTA Study

What has been considered the definitive study about treatment for ADHD was published in late 1999. The US government funded Multimodal Treatment Study of Children with ADHD – "MTA" for short – involved 18 nationally recognized authorities in ADHD at 6 different university medical centers and hospitals to evaluate treatments for ADHD. The study followed 579 elementary school children, aged 7–9, who received either (1) medication alone, (2) psychosocial/behavioral treatment alone, (3) a combination of both, or (4) routine community care.

The study reported that the most effective treatment was a combination of medication and psychosocial/behavioral treatment. Second was medication alone, which was reported as more

effective than routine community care. The drug and behavioral interventions in the study were very intensive. They included training sessions with the parents as well as regular meetings with the child, parents, and even teachers. The regimens also included behavioral therapy in the classroom by a special teacher's aide, and special summer camp for the children. When compared with community-based programs where the doctor would see the child once or twice a year, these intensive study interventions showed improvements over the community-based treatment.

However, all children actually tended to improve over the course of the study, differing only in the relative amount of improvement. For some outcomes that are important in the daily functioning (e.g., academic performance, familial relations), only the addition of behavioral therapy with medication produced improvements better than community care. Of note, families and teachers reported somewhat higher levels of satisfaction for the treatments that included the behavioral therapy components.

In 2007, several follow-up studies of the children in the 1999 study painted a very different picture than that of the initial study. After three years of treatment, there were no significant differences in symptoms among the children who received the intensive drug treatments and those who did not. Further, those on the drug regimens had significantly higher rates of delinquency and substance use [3]. The study also showed that the children in the drug groups experienced growth retardation.

5. Concerns about safety and long-term effects

Though the MTA study showed that behavioral intervention along with medication was shown to be most effective, it was drug treatment alone that most often became the treatment of choice. By 2004, the market for ADHD-related drugs in the USA had grown to over $3 billion annually.

By 2005, concerns were emerging about the safety of the drugs. The FDA announced safety concerns about the drugs causing hallucinations, suicidal ideation, psychotic behavior, and aggressive and violent behavior. The agency convened an advisory panel to examine the safety issues. The panel recommended that "black box" warnings be placed on all ADHD drug products. Black box warnings tell the consumer that the drug has a significant risk of serious or even life-threatening side-effects.

However, after hearings were held, including testimony from doctors who were often consultants paid by the drug makers, the FDA rejected the advisory panel's recommendation. This was the first time in the history of the FDA that the agency rejected an advisory panel's recommendations. But, in 2006, with the evidence mounting about the potentially harmful effects of the medication, the FDA convened a second pediatric advisory panel, with the objective to examine the relationship to cardiac risk including sudden death. This time the FDA took the panel's advice to require black box warnings on the drugs.

Also in 2005, while concerns were surfacing about the safety of the ADHD drugs for children, the makers of Adderall announced the results of a study showing significant improvement in

ADHD symptoms in adults taking the drug. Magazine articles began appearing about adult ADHD (even though at the time ADHD was defined as a disorder of childhood, with symptoms appearing before age 7).

The effectiveness of drug medication continues to be questionable. In 2009, another follow-up study of the MTA groups was published. Eight years after the original intervention, there was again no difference in symptoms among those who continued on medication and those who did not. And those who continued on the medication were about an inch shorter and six pounds lighter than their counterparts who were not on the drugs [4].

At this point, Dr. William Pelham, one of the original researchers of the 1999 study as well as on the follow-up studies, was quoted as saying "The stance the group took in the first paper was so strong that the people are embarrassed to say they were wrong and we led the whole field astray" [5].

There is now growing exploration of the long-term effects of ADHD medication. In early 2010, the Government of Western Australia Department of Health reported on a study it conducted [6]. They described the study as "the first of its type in the world" and found that "long-term use of drugs such as Ritalin and dexamphetamine may not improve a child's social and emotional well-being or academic performance." In a statement, the Chair of the Ministerial Implementation Committee for Attention Deficit Hyperactivity Disorder in Western Australia said "We found that stimulant medication did not significantly improve a child's level of depression, self-perception or social functioning and they were more likely to be performing below their age level at school by a factor of 10.5 times."

In spite of the growing number of studies indicating the questionable long-term effectiveness of ADHD drugs, there has been little abatement in the number of children prescribed these drugs. A recent study of medication trends reported a 36% increase in ADHD prescriptions from 2008–2012, with the number of adults on these drugs growing even faster, with a 53% increase over the same time period [7]. Drug sales continue to grow, expecting to reach almost $13 billion in 2015, and more children identified with the disorder. With no clear understanding of the causes, it raises the question as to whether this is the result of increased prevalence, better diagnostics, or better marketing.

ADHD is now one of the most researched psychiatric disorders of childhood. Usually, such extensive research leads to a more specifically and more narrowly defined description of a disorder. However, with ADHD, the description has grown broader and more inclusive rather than narrower and exclusive, encompassing a wide variety of temperaments, learning abilities, and social and behavioral responses.

6. Alternative treatments and prevention

For some children and adults, ADHD medication can be life-changing. However, like all medication, ADHD drugs do not work for everyone. In general, medication tends to be

effective for some users, not effective for others, and have adverse effects for the remaining users.

Current medications do not cure ADHD. They can help control the symptoms, and can help a child pay attention. It is not clear, however, whether medication helps children learn better. Further, studies do not show long-term functional benefit from medication.

The American Academy of Pediatrics recommends behavioral approaches as the first line of treatment for young children. For elementary school age children and adolescents, if behavioral therapy alone is not sufficient, then medication is recommended – preferably along with behavioral approaches [8]. Though the guidelines recommend behavioral approaches as first-line therapy, or if necessary, both medication and behavioral approaches, less than half of children treated for ADHD receive behavioral therapy. Studies do not show long-term functional benefit from medication. In contrast, behavioral approaches help children learn self-control, critical for functionality and success.

Though millions of adults and children are affected by ADHD, there is little or no study of means of preventing the disorder. While ADHD medication can be effective for a percentage of those with symptoms, medication as prevention would be a dangerous strategy. Studies have shown that for those who do not exhibit symptoms of ADHD and evidence of biochemical imbalance or developmental impairment, these drugs can be harmful. In surveys of nonmedical use, or abuse, of ADHD drugs, adverse events were frequently reported, including sleep difficulties (72%), irritability (62%), dizziness and light-headedness (35%), headaches (33%), stomach aches (33%), and sadness (25%) [9].

Non-pharmaceutical approaches may hold the greatest promise for both prevention and for self-management and learning. Parents and adult sufferers frequently turn to diet and nutrition to treat symptoms following anecdotal reports of the association between food additives, environmental toxins, or nutritional deficiencies, with the expectation that addressing these issues may reduce symptoms or prevent development of ADHD, though there is scant research on the effectiveness. There are however, some alternatives that show promise as both treatment approaches and as potential means of prevention. These will be discussed in the following sections.

7. Omega-3

One notable dietary supplement that has shown research-based benefits is the use of omega-3 fatty acid supplementation [10, 11]. Omega-3 increases myelination, development of a fatty layer around the cell fibers. Myelination increases the speed of information processing. Studies have shown that those with developmental delay in motor and cognitive milestones have significant reductions in myelination [12], offering an explanation for the mechanisms of how omega-3 can improve symptoms of ADHD. Since omega-3 fosters development of myelination, and myelination increases brain processing, supplementation with omega-3 may offer a viable preventive approach.

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8. Sleep

Insufficient rest can have serious detrimental effects on learning, mental health, and brain development, including memory. Memory reprocessing during sleep is an important component of how our memories are formed and ultimately shaped [13]. Studies show that sleep facilitates learning, theoretically because it prevents interference from on-going sensory input and cognitive activities that normally occur during waking. Similarly, research has shown that restful waking (e.g., lying in a dark room) also facilitates learning, and can contribute to the facilitation of learning that occurs during sleep [14].

A study of behavioral sleep intervention modestly improved the severity of ADHD symptoms in a community sample of children with ADHD, most of whom were taking stimulant medications. The intervention also improved the children's sleep, behavior, quality of life, and functioning, with most benefits sustained to six months post-intervention [15].

Study of sleep duration found that children having longer duration of sleep per night were at lower risk of ADHD symptoms than those who slept only 7.7 hours or less [16]. Thus, improving the quality of sleep and duration of sleep can have important implications for reduction of ADHD symptoms including behavior regulation and executive function, and importantly, for reducing the risk of ADHD.

9. Stress

Stress can play a significant role in ADHD symptoms. Stress interferes with executive function and behavior regulation [17, 18], resulting in difficulties with working memory, organization, attention, and impulse control. Stress also limits mental flexibility and reduces coping strategies.

Many of the symptoms associated with ADHD are also symptoms of chronic stress (Table 1). The Diagnostic and Statistical Manual of Mental Disorders (DSM-V) symptoms of ADHD can be viewed as the way in which these symptoms appear in children.

Symptoms of Stress	Symptoms of ADHD
Inability to concentrate	Difficulty sustaining attention Not listening when spoken to
Difficulty organizing	Difficulty organizing
Memory problems	Forgetfulness
Poor judgment	Speaks without thinking
Short temper	Impulsivity

Table 1. Symptoms of stress closely match symptoms of ADHD

The part of the brain responsible for developing means of adjusting to stress is the prefrontal areas. Children with ADHD have been shown to have impaired function of this area [19]. This

region is responsible for developing coping strategies, influencing the ability to handle stress. Children exposed to trauma or other adverse experiences during childhood are almost three times more likely to have ADHD. Chronic acute stress leads to elevated levels of cortisol. In children with ADHD, high cortisol levels interfere with executive function, self-regulation, and learning [20].

Chronic physical or psychological stress can change the brain. The body's natural response to stress is to activate the sympathetic nervous system, or "fight or flight" response. This results in changes to the levels of dopamine, norepinephrine, serotonin, and cortisol. These changes interfere with memory, and lead to increases in irritability, aggression, impulsivity, suicide, and alcohol and drug abuse. Chronic stress damages or kills brain pathways. As much as 34% reduction in cells in the prefrontal cortex have been reported [21]. Modalities that reduce stress can have a positive effect on ADHD symptoms.

In addition, early intervention with stress-reducing strategies in the presence of trauma, emotional or physiological stress, or even severe illness, has the potential to prevent the development of ADHD symptoms. Recognition of the relationship of stress and the symptoms of ADHD helps to understand the underlying factors influencing these symptoms, and helps improve screening and treatment approaches.

10. Stress reduction and meditation

Given the role stress seems to play in the cognitive function and symptoms of ADHD, it is logical to explore stress reduction techniques as a means of minimizing the effects of stress and potentially preventing ADHD. Commonly suggested stress management options include exercise, deep breathing, yoga, and meditation. Research in techniques is limited, but meditation shows promise as both a behavioral strategy for treatment and as prevention through stress reduction.

Recent neuroscience research has shed light on the differences in different forms of meditation, how they work, the areas of the brain affected, and the overall effects. Different techniques use different procedures for reaching a state of relaxation, and have different effects [22, 23].

Meditation practices have been classified into three types based on their EEG results. The three types are (1) techniques of concentration, also called focused attention, (2) mindfulness-type meditation, also called open monitoring, and (3) transcending, also called automatic self-transcending [24].

Techniques of focused attention are concentration techniques, where attention is kept on the object of meditation, such as an event, image, or sound. Open monitoring or mindfulness-based techniques involve dispassionate non-judgmental monitoring of experience. Automatic self-transcending meditation is defined as effortless transcending of the meditation process itself [24, 25]. Each of these techniques has their own unique EEG signatures.

Preliminary research investigated the effects of mindfulness training on 24 adults and 8 adolescents diagnosed with ADHD, who received an 8-week mindfulness training program.

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Seventy-five percent of these individuals finished the eight-week program. After the mindfulness training, both adults and adolescents exhibited statistically significant decreases in inattention and hyperactivity [26].

The Transcendental Meditation (TM) technique falls into the category of automatic self-transcending [27]. Concentration and open monitoring meditations both require some mental effort (i.e., holding attention on its object or maintaining attention on an on-going experience, respectively). The Transcendental Meditation technique automatically leads to a relaxed state where the mind is not actively engaged in controlling or directing the thinking process. The awareness actually goes beyond the active level of thought to experience what is referred to as transcendental or pure consciousness.

Transcendental Meditation is practiced for 10–20 minutes twice a day, with eyes closed. The technique is simple, and easy to do. It does not involve concentration or controlling the mind – both of which are difficult for an individual with ADHD.

Measurement of brain function during the Transcendental Meditation technique shows increases in brain coherence both during the practice of the Transcendental Meditation technique and afterwards in activity [24, 28, 29]. The primary areas of the brain activated are the frontal and prefrontal executive areas responsible for attention, executive function, emotional stability, and anxiety (Figure 1) [28, 30].

Study of college students practicing the Transcendental Meditation technique showed reduced stress and anxiety, and improved cognitive processes compared to controls [31, 32]. Effects include balancing the neurohormones including cortisol and serotonin [33, 34, 35] during meditation and during activity.

The use of the Transcendental Meditation technique for stress reduction in adolescents has resulted in improvement in school behavior, decreases in absenteeism and rule infractions, and reduction in suspensions due to behavior-related problems [36]. Students practicing the Transcendental Meditation technique show increased emotional regulation and improved well-being [37], as well as improved academic performance.

Students with ADHD who were practicing the Transcendental Meditation technique in school showed reduced stress and stress-related symptoms including anxiety, anxiousness, and depression. Improvements in behavior regulation and emotional control were also significant. In addition to reduction in stress-related symptoms, there were improvements in cognitive function, including the ability to initiate tasks, working memory, planning, and organizing.

In an effort to more objectively diagnose ADHD, rather than completely relying on subjective questionnaires, the US Food and Drug Administration (FDA) recently approved a device for measuring brain waves that can be used as a means of diagnosing ADHD. The device measures theta/beta brain frequencies ratio. Theta/beta ratios are higher in children with ADHD.

The Transcendental Meditation technique has been shown to improve theta/beta ratios through the effortless practice of the technique. In a randomized controlled trial of the Transcendental Meditation technique, EEG coherence, theta/beta ratio, and executive function were measured in middle school students with ADHD. After three months, the group

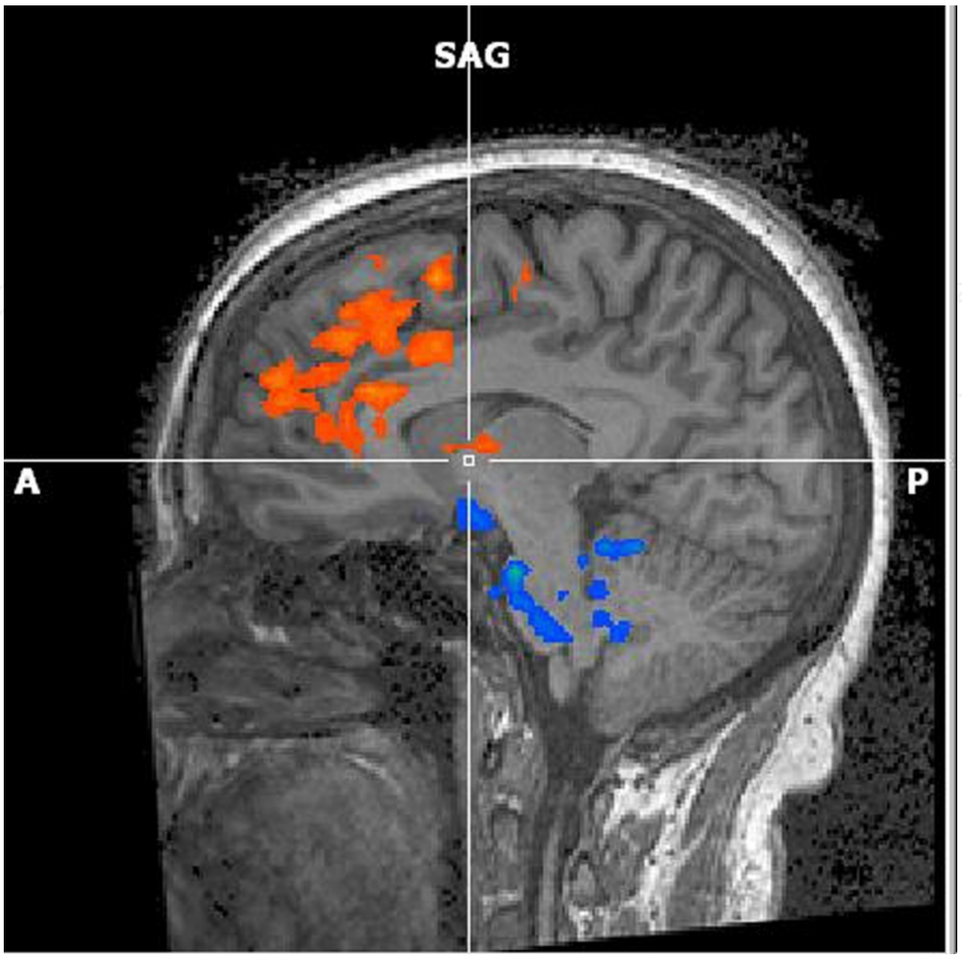

Figure 1. fMRI showing increased activation in the frontal areas of the brain during the practice of the Transcendental Meditation technique (Courtesy of M. Ludwig, 2012)

practicing the Transcendental Meditation technique showed improvements in theta/beta ratios. At the 6-months post-test, theta/beta ratios were in the normal range [38].

11. Conclusion

Understanding the history of the development of diagnostic criteria for ADHD, the parallel growth of the ADHD drug market, and factors that improve the symptoms of ADHD provides insight into alternative approaches to treatment and the potential for prevention.

Recognition of the role fatty acids, sleep, and stress play in cognitive function and behavior regulation in ADHD offers opportunities to intervene to alter the course of the disorder. Interventions that immediately address reducing the effects of the stressors, improve sleep, and enhance myelination have the potential of reducing the damaging effects on the brain, and possibly avoiding manifestation of the symptoms of ADHD.

Initial research supports the value of Transcendental Meditation as a promising behavioral tool not only for reducing symptoms of ADHD in adults and children but also for enhancing brain development, and for potentially preventing the future development of symptoms. Strategies for improved sleep and omega-3 dietary supplementation may also be beneficial strategies for intervention and prevention.

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