

Attention-deficit hyperactivity disorder: preventing overdiagnosis and overtreatment

Déficit de atenção e hiperatividade: prevenindo o sobrediagnóstico e o sobretratamento

Déficit de atención e hiperactividad: previniendo el sobrediagnóstico y el sobretratamiento

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Abstract

The first part of this article focuses on the wide variations in the diagnosis of attention-deficit hyperactivity disorder (ADHD) that are observed between countries and between regions within the same country. Diagnosing ADHD is more problematic than is commonly thought. For instance, younger American children in the same grade at school are 64% more likely to receive the diagnosis and symptoms can result from many underlying causes. Furthermore, ADHD can be confused with many other health issues. As a result it is largely overdiagnosed and overtreated. The second part of the article reviews recent studies showing that anti-ADHD drugs lack long-term effectiveness and come with important adverse events. Overall, and in the long run, the pharmacologic treatment of ADHD is likely to cause more harm than good.

Resumo

A primeira parte deste artigo concentra-se nas grandes variações no diagnóstico de transtorno de déficit de atenção e hiperatividade (TDAH), que são observadas entre países e entre regiões de um mesmo país. O diagnóstico de TDAH é mais problemático do que normalmente se pensa. Por exemplo, crianças norte-americanas mais jovens no mesmo grau escolar são 64% mais propensas a receber o diagnóstico e os sintomas podem resultar de muitas causas subjacentes. Além disso, o TDAH pode ser confundido com muitas outras questões de saúde. Como resultado, o TDAH é amplamente sobrediagnosticado e sobretratado. A segunda parte do artigo revisa estudos recentes que mostram que as drogas anti-TDAH não têm eficácia de longo prazo e contam com eventos adversos importantes. No geral, e no longo prazo, o tratamento farmacológico do TDAH é susceptível de causar maiores danos do que benefícios.

Resumen

La primera parte de este artículo se centra en las amplias variaciones en el diagnóstico del trastorno de hiperactividad por déficit de atención (TDAH) que se observan entre países y entre regiones dentro de un mismo país. El diagnóstico de TDAH es más problemático de lo que se piensa comúnmente. Por ejemplo, los niños estadounidenses más jóvenes en el mismo grado en la escuela son 64% más propensos a recibir el diagnóstico y los síntomas pueden ser el resultado de muchas causas subyacentes. Además, el TDAH se puede confundir con muchas otras cuestiones de salud. Como resultado, el TDAH es ampliamente sobrediagnosticado y sobretratado. La segunda parte del artículo revisa estudios recientes que muestran que las drogas anti-TDAH carecen de eficacia a largo plazo y cuentan con eventos adversos importantes. En general, y en el largo plazo, el tratamiento farmacológico del TDAH es probable que cause más daños que beneficios.

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Introduction

Close to one child out of five has been diagnosed with attention-deficit hyperactivity disorder (ADHD) in Kentucky.¹ At the other end of the spectrum, Cohen and many others consider that it is not a valid mental disorder,² and according to *Der Spiegel*, psychiatrist Leon Eisenberg, the 'scientific father' of ADHD, declared a few months before he died that 'it is a prime example of a fictitious disease'.³ It is not our purpose here to address this specific aspect of the debate although some children do have problems of inattention, impulsivity and hyperactivity and do need help. Our purpose here is to argue that 'ADHD' is largely overdiagnosed and overtreated, which most likely causes more harm than good.

Variations that cast a long shadow over the diagnosis

In the last two decades, rates of ADHD have skyrocketed, especially in the United States, with a tenfold increase in the use of medications.⁴ The market for anti-ADHD drugs went from \$15 million in the mid-nineties to \$9 billion in 2012.⁵

Wide variations in diagnosis have been observed between countries. In France, the *Haute Autorité de Santé* (HAS) estimates prevalence at around 2%.⁶ The Centers for Disease Control and Prevention report that 11% of children 4-17 years of age received an ADHD diagnosis by a health care provider in 2011.¹ Furthermore, prevalence varies extensively by state, from a low of 5.6% in Nevada to a high of 18.7% in Kentucky.¹ In Québec, close to 13% of high school students have had an ADHD diagnosis confirmed by a doctor. In the United States, boys are 2.4 times more likely to be diagnosed than girls,¹ while in Québec 16% of boys received the diagnosis, versus 9% for girls.⁷

Prevalence also varies according to the diagnostic tool used. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM) generally gives rise to rates between 5% and 10%, while the International Classification of Diseases (ICD) of the World Health Organisation gives rise to rates varying from 0.4% to 4.2%,⁶ which is 2.5 to 13 times less for ICD, whose criteria are much more restrictive.⁸ Insofar as France is concerned, it uses *The French Classification of Child and Adolescent Mental Disorders*.

These wide variations are indicative of the subjective nature of the diagnosis, which explains, in part, why it is so controversial. Adding to the controversy, it has never been proved that it is a genetic disorder implying a deficit of dopamine⁹. Indeed, David Kupfer, Chairman of DSM-5, concedes that 'biological and genetic markers that provide precise diagnoses that can be delivered with complete reliability and validity [are still] disappointingly distant'. In other words, there are no such things as biological markers for any DSM diagnosis.¹⁰

There is more than we might think when it comes to diagnosing ADHD. The Attention Deficit Clinic of Rivière-des-Prairies Hospital in Montréal receives patients referred by a doctor suspecting or having diagnosed ADHD. In 2006, after evaluation, close to 40% of diagnoses were withdrawn;¹¹ recently, that figure has gone up to 60%.^a

There is clear evidence and many compelling reasons to believe ADHD is overdiagnosed. First, inattention, impulsivity and hyperactivity are common among young children and adolescents. Where do we put the cursor between what's 'normal' and what's not? Second, it is easily confused with some developmental disorders like dyslexia and many medical conditions such as apnea; third, these symptoms can be the result of many underlying causes, like stressful living conditions, ecological hazards, etc.; fourth, the criteria outlined in DSM are redundant giving the diagnosis a false sense of validity.

A question of maturity or ADHD?

Children in the same grade at school may almost have a year in age difference. For the United States, Todd Elder's study showed that 8.4% of children born just before the cut-off date for kindergarten eligibility (kids five to six) are diagnosed with ADHD, compared to 5.1% of children born in the month after the cut-off date.¹² In other words, the youngest and most developmentally immature children are 64% more likely to be diagnosed with ADHD. The consequences are far reaching: 'the youngest children in fifth and eighth grades are nearly twice as likely as their older classmates to regularly use stimulants prescribed to treat ADHD'.¹² About one million kids are potentially overdiagnosed or misdiagnosed. This is consistent with what was found in Iceland. In a group of children 7 to 14 years of age, the youngest in their class were 50% more likely to be diagnosed with ADHD.¹³ The younger the child, the more he or she is likely to be overdiagnosed.

The identification of what looks like ADHD symptoms in grade one is a poor predictor of ADHD later on. A Swedish study screened 422 first graders by asking parents and teachers to answer the Conners 10-item scale on ADHD. Half the first graders who screened positive 'ended up with a formal diagnosis in the fourth grade'.¹⁴ Guidelines from the US National Institute of Mental Health (NIMH) instructing health professionals, and ultimately teachers, were used to evaluate ADHD by comparing children in the same grade at school, are another driver of overdiagnosis.

Mild to moderate ADHD?

According to Centers for Disease Control and Prevention, 86% of kids would have mild to moderate ADHD, which represents an important pool of potential overdiagnosis. Mild or moderate symptoms could easily be confused with normal behavior and with the fact that school might not be adapted to the needs of a lot of children. Many children are more active and less attentive than average. Does that mean they are disordered? Moreover, as happens relatively frequently with DSM, many are diagnosed without fulfilling diagnostic criteria.¹⁵ Many times the diagnosis does not take into account the impairment criterion. When researchers considered this factor instead of focusing on symptoms only, they reduced the 16.1% prevalence of ADHD to 6.8%.¹⁶ In North Carolina, after applying the impairment criterion, researchers estimated that 6.2% of children (n=1 422) met ADHD criteria while 7.3% were using stimulants; 'over 57% of those who received medication did not meet the criteria'.¹⁷

The distinction between mild to moderate and severe forms is left to the subjective judgment of health professionals since there are no tests or criteria to distinguish between severe ADHD and its 'light and moderate' forms. In many instances, the diagnosis is made in sub-optimal conditions. Swanson's estimate of 1% 'real ADHD' is based on three trained observers seeing the same thing.⁸ What is worrisome is that the severity of symptoms does not seem to really impact the type of treatment, since 87% of children who had an ADHD diagnosis in the United States were medicated in 2010.¹⁵

Is it ADHD, a developmental issue, a somatic problem?

Inattention, impulsivity and hyperactivity can easily be confused with a developmental disorder like dyslexia. Furthermore, many studies have shown a link between sleeping difficulties due to apnea, tonsils,¹⁸ hearing or sight problems and ADHD symptoms. During his 50 years of practice, neurologist Richard Saul was confronted with this problem frequently: 'Over the course of my career, I have found more than 20 conditions that can lead to symptoms of ADHD, each of which requires its own approach to treatment'.¹⁹

Is it ADHD or something else? The problem of comorbidity

The Canadian ADHD Resource Alliance (CADDRA) estimates that 87% of children get at least two diagnoses and 67% at least three.²⁰ Among those are: generalized anxiety, major depression, conduct disorder, oppositional defiant disorder, etc. As a result, many children and adolescents are polymedicated with potentially disastrous consequences, since each additional drug increases the risk of adverse events.

The problem of comorbidity raises many questions. First, DSM diagnoses are considered discrete entities with more or less clearly defined borders, an idea which has been widely challenged. You may have a cardiovascular disease, pneumonia and osteoarthritis. These are three different illnesses and tests are available to diagnose them, but there are no tests for DSM diagnoses. When a child gets an ADHD diagnosis with generalized anxiety and major depression, does he or she have three different illnesses or are these three different expressions of the same suffering? What is disturbing, at least in Québec, is that a doctor can overbill if his patient gets more than one diagnosis and/or when he or she administers scales used to diagnose ADHD.

Second, do inattention and hyperactivity come first or are they the result of something else, like stressful living conditions (overwhelmed parents, dysfunctional families, a difficult divorce, child abuse, lack of support, poverty)? It is well known that poverty generates a lot of stress. One of the pioneers of ADHD research in the United States, Alan Sroufe, followed

kids from poor neighbourhoods for many years; he observed that they are 75% more likely to be diagnosed with ADHD than the national average.²¹ It's normal for kids coming from poor and/or dysfunctional families to feel anxious, moody, hyperactive or inattentive. You have to look for underlying causes: social, ecological, medical, iatrogenic and likely dietary. Some recent studies have brought evidence that pesticides, heavy metals, pollution, exposure to cigarette smoke in the womb, can induce ADHD-like symptoms.²² Third, the criteria for an ADHD diagnosis are flawed. The inattentive type requires six out of nine criteria which are summarized in Table 1.

Table 1. DSM-5 criteria for ADHD, inattentive type.

1.	'Often fails to give close attention to details.
2.	Often has difficulty sustaining attention in tasks or play.
3.	Often does not seem to listen when spoken to.
4.	Is often easily distracted by extraneous stimuli.
5.	Is often forgetful in daily activities.
6.	Often does not follow through on instructions.
7.	Often has difficulty organising tasks and activities.
8.	Often avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort.
9.	Often loses things necessary for tasks or activities.'

Source: American Psychiatric Association, DSM-5, p. 59.

DSM-5 has added more examples, but the criteria have not changed. However it has changed the age for symptom onset from seven years of age to 12, which increases the risk for more overdiagnosis. The purpose of multiple criteria is to raise the threshold for a diagnosis, '... making it appear that the *DSM* standards will ensure validity'.²³ A careful reading reveals that the first five criteria are redundant. After the first criterion, each of the following four essentially repeats the first: the subject is inattentive because he lacks attention in different contexts. It looks more like a tautology than different criteria. The same remarks go for the impulsivity and hyperactivity type. Furthermore, why six symptoms out of nine? Why not five or seven? And what is meant by 'often'?

By focusing on symptoms the individual is cut off and isolated from what defines him, his social, ecological and psychological environment. He is reduced to the role of carrier of symptoms and separated from what makes every one of us a human being.

A good part of the psychiatric establishment has disqualified or taken its distance from DSM. For diametrically different reasons, outside of the scope of this article, Thomas Insel, director of the National Institute of Mental Health, has disqualified DSM because it is using symptoms as a basis for diagnosis.²⁴ His stance has created a real storm in the world of psychiatry. Allen Frances, editor-in-chief of DSM-IV, pressed for a boycott of the latest version of the manual;⁵ in 2007, Robert Spitzer who presided over the destinies of the third version has taken its distance from the 'bible', admitting that many disorders included in DSM-III might be normal reactions.²⁵

Effectiveness of anti-ADHD drugs

Experience and short-term trials sponsored by drug makers have shown that anti-ADHD drugs increase attention, memory, note-taking, etc. From these observations, pharmaceutical promotion resolved that anti-ADHD drugs improve academic results and behaviors, protect against losing employment, delinquency and crime. These risks are supposedly greater than the risks of adverse drug events from psychostimulants. In 2008, FDA sent a warning letter to five manufacturers of psychostimulants asking them to withdraw claims that psychostimulants improve academic performance:

*'This presentation is misleading because it implies that use of Concerta will lead to an improvement in academic performance throughout the day when this has not been shown by substantial evidence or substantial clinical experience.'*²⁶

The long-term effectiveness (in real life as opposed to 'efficacy' in clinical trials) of psychostimulants has been challenged by non-industry long-term studies. The first one is the famous 1999 Multimodal Treatment ADHD study (MTA), sponsored by the National Institute of Mental Health. It recruited close to 600 subjects divided in four groups: (1) Drug only; (2) Therapy

only; (3) Combination of 1 and 2; (4) Usual care, (67% were on stimulants). The first phase lasted 14 months and the children were followed-up for eight years. To the dismay of the authors, the follow-up conclusions were very different from the initial ones. At 14 months they found that medicated children had better outcomes, but 10 months later, at two years: 'Approximately half of the initial advantage had dissipated'; and at three years 'treatment groups did not differ significantly on any measure'.²⁷ The 'psychiatric, academic or social functioning outcomes' were no different, and kids on ADHD drugs fared no better in spite of increasing the dose by 41%. Moreover, from the beginning, the blinded observer did not find differences between groups on most measures.

The Raine study came out in 2010. It was sponsored by the Western Australian government. It was a longitudinal study of 2878 children ages six to 14 followed for eight years. Among them, 131 were diagnosed with ADHD. The children diagnosed with ADHD and receiving psychostimulants were 10.5 times more likely to be failing school than those with ADHD and never medicated. Those who were medicated had slightly worse outcomes in terms of depression, social functioning and self-esteem; and very importantly, those who were medicated on a regular basis had a diastolic blood pressure 10.79 mm HG higher than children who never received medication.²⁸ Although the risk is lower for children, according to a study published in *Lancet* in 2002, '...increases in diastolic blood pressure of more than 1 mm Hg raise the risk for heart attack by 10 percent and stroke by 7 percent in middle-aged adults...'.²⁹

Janet Currie from Princeton University and her team used a Canadian longitudinal study that followed children for 14 years. The results published in 2013, showed that those who were medicated were more liable to repeat grades, had worse results in maths, experienced a deterioration of relations with parents, exhibited slightly more anxiety, depression and sadness, especially girls.³⁰ Children in Québec, where proportionally more stimulants are prescribed, fared worse than those in the rest of Canada.

Finally, the follow-up of the Preschool ADHD Treatment Study (PATS), sponsored by NIMH, published in 2013, determined that psychostimulants did not work for 89% of pre-school children. After six years, most of those who were medicated exhibited a little more (a few percentage points) ADHD symptoms than those who were not.³¹

Adverse drug events

Some adverse drug events of psychostimulants are well-known: stunted growth, reduction in appetite, increase in insomnia, anxiety, irritability and emotional outbursts. In the MTA study, 11% stopped treatment because of moderate to severe side effects. In 2010, a survey of 325 participants indicated that 48% reported at least one side effect, most often loss of appetite, insomnia and mood swings. Twenty-one percent were considered 'very bothersome' or 'extremely bothersome'.³²

In Canada, the *Toronto Star* put a lot of effort into getting a data base from Health Canada. Over a ten-year period, the regulator received close to 600 notifications of serious adverse events where anti-ADHD drugs are the number one suspect. David Kessler, formerly FDA commissioner, considered that 1% of serious adverse events are reported.³³ Here is an incomplete list of serious adverse events: seven suicides, 76 suicide attempts, 24 convulsions, 48 hallucinations, 28 cardiac problems, 23 liver complications.³⁴ More than half of these cases were reported during the last two years before 2012.

Between 2008 and 2012, FDA received many reports of serious adverse drug events in children under age 18, concerning two stimulants, lisdexamfetamine (Vyvanse) and methylphenidate (Concerta), as well as atomoxetine (Strattera) which is a failed antidepressant recycled as an anti-ADHD drug. These three drugs were listed among the 15 for which adverse reactions were most frequently reported. Table 2 summarizes those events.

Atomoxetine shares a suicidal behavior warning with other antidepressants, but not the stimulants. The three have warnings about psychosis and hallucinations. The prescribing information contains a warning about sudden death for methylphenidate but 'the literature is mixed'.³⁵ Cardiac events (chest pain, syncope, QT interval prolongation) were reported with atomoxetine. Seventeen cases of movement disorders were reported with lisdexamfetamine. These reports do not prove a causal relation between the drug and the adverse event. However, their multiplication is a sure sign that these events are not pure coincidences and that something is amiss and warrants thorough investigation and circulation of the information.

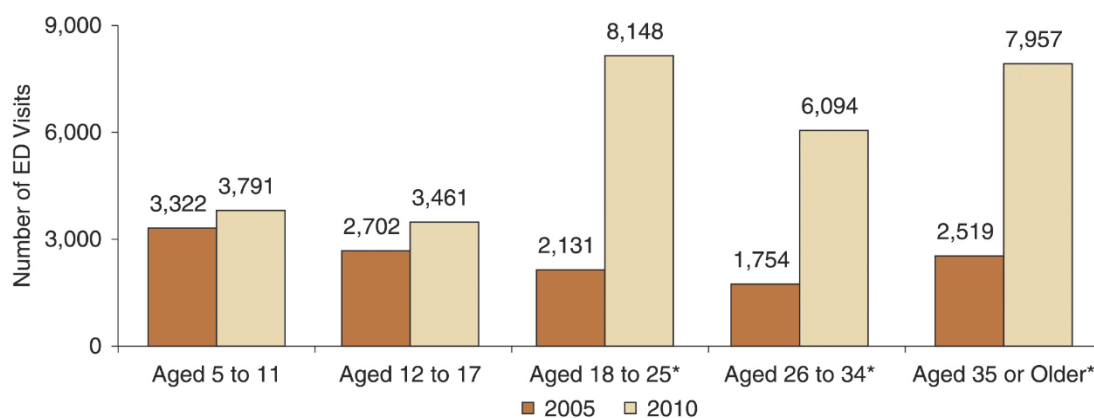
Table 2. Most frequent serious adverse reactions for three anti-ADHD drugs, 2008-2012.

Rank	Drug name	No. of cases	Most freq ADR	2 nd most freq ADR
6	Methylphenidate (Concerta)	418	Sudden death	Aggression
8	Lisdexamfetamine (Vyvanse)	314	Suicidal ideation	Aggression
12	Atomoxetine (Strattera)	227	Suicidal ideation	Chest pain

Source: Institute for Safe Medication Practices, Quarter Watch, Monitoring FDA MedWatch Report. Available at: www.ismp.org/QuarterWatch/, January 16, 2014.³⁵

In the last few years the number of emergency visits has mushroomed especially among people 18 and older. The figures in Graph 1 are from a branch of the US Department of Health and Human Services. Emergency room visits involving nonmedical use made up half of visits and nearly tripled during this time to close to 15600.³⁶

A consortium of psychostimulants manufacturers opposed the suggestion by the European Medicines Agency to test their safety in long-term studies.³⁷ If the adverse events linked to anti-ADHD drugs are banal and if the benefit/risk profile is favorable why object to such a study?



*The change from 2005 to 2010 is statistically significant at the .05 level.

Source: 2005 and 2010 SAMHSA Drug Abuse Warning Network (DAWN).

Graph 1. Emergency visits after taking Anti-ADHD drugs. United States, 2005-2010. Source: Substance Abuse and Mental Health Services Administration, <http://www.samhsa.gov/data/2k13/dawn073/sr073-add-adhd-medications.htm>, January 2013.³⁸

Alternatives

There are well documented alternatives to medication for children who experience problems of inattention and hyperactivity: parent training, social skills training, cognitive control, and so on.

Conclusion

There is clear evidence that ADHD is overdiagnosed. If anti-ADHD drugs are efficient in the short term, they lose this capacity in the medium to long-term. These drugs are linked to some serious adverse events. Their profile benefit/risk is likely negative.

Note

- a. Personal communication by Joël Monzée, doctor in neurology and psychotherapist.

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