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Chapter 10

The Manipulation of Data and Attitudes about ADHD: A Study of Consumer Advertisements

Jonathan Leo and Jeffrey Lacasse

At this point in time, Direct-to-Consumer Advertising (DTCA) is only legal in the United States and New Zealand, but various commercial and political groups are actively seeking to legalize DTCA in Europe, Canada, and beyond (Priest, 2007). Recently, officials from the US White House have put pressure on the British government to allow DTCA (Boseley, 2006). As the medical establishments in the United Kingdom and Canada consider the potential ramifications of legalizing DTCA, it is valuable to consider the example of the United States, where such advertisements have been legal and widespread since 1997. In America, consumer advertisements are now ubiquitous and have become an integral part of popular culture. In many cases, the content of these advertisements may be taken as fact, despite a major disconnect between their slogans and the scientific literature (Lacasse and Leo, 2005; Lacasse and Leo, 2006a; Lacasse and Leo, 2006b).

In 1996, the pharmaceutical companies spent $791 million on consumer advertising, and by 2000 they were spending $35.1 billion (NIHCM Foundation, 2000). Paralleling this widespread increase of DTCA in America there has been a dramatic rise in the number of children diagnosed with ADHD and subsequently prescribed stimulant medication. Between 1994 and 1999, the production of Ritalin™ increased eight hundred percent, with ninety percent of

it being consumed in the United States (See chapter ten by Hart for a more complete discussion of diagnostic rates). The purpose of this chapter is to examine the scientific evidence behind the statements made in psychostimulant advertisements, keeping in mind that patients look to their physicians to contextualize these advertisements, the scientific literature, and each patient's unique situation.

DTCA and the increased use of Ritalin™

A major goal of DTCA is to start a conversation, initiated by the patient and then elaborated on by the physician. According to one advertising executive, the goal is 'to drive patients to their doctor' (Loden and Schooler, 1998). Patients who have seen an advertisement for a disease are more likely to bring up any concerns about a potential symptom with their doctor. The proponents of DTCA point out that, from a public health perspective, this is beneficial because increased disease awareness in the general population results in more people being treated (Cutler, 2005). Implicit in this line of reasoning is that the consumer advertisements are accurate. If the advertisements are inaccurate, then the doctor-patient relationship is greatly complicated, as an explanation by a physician that differs from the information disseminated by the advertisements would be met with resistance and confusion by the patient.

The example of ADHD is particularly interesting to those following the proliferation of the consumer advertisements, for several reasons: ADHD has been the subject of considerable controversy over the years. It has no biological diagnostic markers; it has been theorized to be over-diagnosed in Western countries; and it can be treated by both psychosocial and pharmacological interventions. In addition, the most popular treatments for ADHD are Schedule II pharmaceuticals – psychostimulant drugs, such as methylphenidate or amphetamine, which carry both addictive properties and the risk of iatrogenic harm, and are largely prescribed to a vulnerable population – children – through proxy authorization and recommendation by their parents. In the early adoption of DTCA, adverts for such products were seen as unlikely, but have subsequently become commonplace in popular culture. There are now repeated advertising campaigns in mainstream magazines that promote psychostimulant treatment of children directly to parents. In addition, the emergence of the World Wide Web has provided a major venue for DTCA. Googling 'ADHD,' now inevitably links users to DTCA websites that promote psychostimulants.

Underlying any discussion of ADHD, and what every neuroscience researcher is aware of, is the understanding that the most straightforward experiment in all of neuroscience is the one seeking to determine if Ritalin™ works. Here, 'works' is defined as a short-term improvement in attention span. Whether the subjects are male or female, preschoolers or geriatrics, diagnosed with ADHD or not, given medication by a doctor or a friend, one point has been known for 75 years: stimulants improve anyone's and everyone's ability to pay attention.

As a case study in DTCA, we examined the presentation of several complex aspects in consumer advertisements about ADHD, such as neuroimaging, genetics, medication efficacy, and the chemical imbalance theory. For each topic presented in web-based or print advertisements, we looked at the evidence in the medical literature, and asked whether the advertisements accurately reflected the scientific literature. We focused on how practicing clinicians would have to explain to their patients – or patients' parents – that, contrary to the advertisements, scientists still have not answered these complex questions:

> *While the specific cause has not been confirmed, brain imaging research using a technique called magnetic resonance imaging (MRI) has shown that differences exist between the brains of children with and without ADHD* (Ritalinla.com).

Radiological images of the brain have become a powerful aid in the marketing of ADHD medications, as the images are believed to document the existence of a definable and visible neuropathological abnormality. The brain imaging pictures usually contrast a brightly coloured 'normal' brain to a slightly dimmer 'ADHD' brain (Rosack, 2004). However, the ADHD neuroimaging studies are plagued by a significant confounding variable. In the overwhelming majority of the ADHD imaging studies the ADHD children have had a prior history of medication use, making it extremely difficult to know if the reported differences between ADHD children and controls result from an idiopathic organic brain defect – as implied or stated in most studies' advertisements – or from brain changes resulting from prior drug use by the ADHD subjects (Giedd, Blumenthal, Molloy and Castellanos, 2001; Leo and Cohen, 2003).

For some scientists (National Institute of Mental Health, 2002), the issue of prior medication use was settled with the publication of a NIMH-sponsored study in 2002 (Castellanos *et al.*, 2002), which

included a group of non-medicated ADHD children. The authors concluded that the brains of children with ADHD were three percent smaller than control brains. In addition, based on a comparison between the medicated and non-medicated ADHD children, the authors concluded that the medications were not responsible for the volume reductions. Yet, what could have been a simple comparison was confounded by the fact that, on average, the non-medicated ADHD subjects were two years younger than the control subjects. Prior to the publication of this study, a common justification by ADHD imaging researchers for using medicated ADHD subjects in their studies was that it was difficult to find non-medicated ADHD children. However, this does not explain why once a group of non-medicated ADHD children was identified, it suddenly became difficult to find age-appropriate controls.

In 2003, a second NIMH-sponsored study was published that also included medicated and non-medicated ADHD patients, yet, surprisingly, this study did not report on the comparison between these two groups; instead, the researchers combined the medicated and non-medicated children together into one ADHD group (Sowell *et al.*, 2003). Their justification for not reporting on the comparison between medicated and non-medicated ADHD children was the lack of uniformity between the subjects regarding medication -something which the first NIMH study never commented on. Since replication is an essential component of the scientific process, it is unclear why the comparison between the medicated and non-medicated ADHD children, which was considered so significant in the first NIMH study, was not deemed worthy of publication for the second NIMH study.

Leaving any specific criticism of the experimental design of these studies aside, there is a much broader problem with the brain imaging studies that makes interpretation of even well-controlled imaging studies more complex than what is portrayed in one-page advertisements, namely, differences do not necessarily equal disease. Even if a large number of children have a brain that is slightly 'different' than the average brain (and this group is getting larger every year), this fact does not necessarily lead to the conclusion that these children have a disease requiring medication. All behavioural traits fall onto a spectrum, and even if brain scans can eventually be used to identify which children belong at the ends of the spectrum, answers about how many children to medicate, whether it is three, five, or twelve percent of school-aged children, cannot be found in a radiological image.

For instance, Joseph Rey and Michael Sawyer, in *The British Journal of Psychiatry*, ask the question, 'Are Psychostimulant Drugs Being Used Appropriately to Treat Child and Adolescent Disorders?' (Rey and Sawyer, 2003, p. 284). They point out that the National Institute for Clinical Excellence (NICE) only recommends methylphenidate for children diagnosed with the severe hyperkinetic disorder and not for children with the inattentive or impulsive-hyperactive subtype, a guideline that only includes about one percent of the children in the community. Yet, the American Academy of Pediatrics casts a bigger net and states that even children with the inattentive or impulsive-hyperactive subtype should be given stimulant medication and/or behavioural therapy. Their net could potentially result in seventeen percent of the male children in the population being medicated.

In 2005, the *New York Times* interviewed several leaders in the field of ADHD imaging research who acknowledged the shortcomings of their field. According to the *Times*, 'imaging technology has not lived up to the hopes invested in it in the 1990s,' and, moreover, 'some experts say that the technology has been oversold as a psychiatric tool' (Carey, 2005).

Neurotransmitters

Research suggests an imbalance in the levels of dopamine and norepinephrine, two neurotransmitters (substances that may transmit messages in the brain), may account for many of the signs and symptoms of ADHD (Adderall.com, 2006).

ADHD medications are thought to influence the balance of norepinephrine and dopamine in the brain, helping to improve functioning to more normal levels (Concerta.net, 2008).

Studies show that the brains of children with ADHD may function differently than those of other children. These children may have an imbalance of chemicals in the brain that help to regulate behavior (Ritalinla.com, 2008).

Attention Deficit Hyperactivity Disorder (ADHD) is a common medical condition... Studies have shown that the brains of people with ADHD may work differently, perhaps because of a chemical imbalance (FocalinXR. com, 2008).

After reading these statements, the parents of a child with ADHD could hardly be faulted for requesting a 'Neurotransmitter Level Test,' leaving the doctor to explain the following: (1) the chemical imbalance theory is more 'metaphor' than scientific fact; (2) there is no valid test for neurotransmitter levels; (3) there are no scientific studies that have documented altered neurotransmitter levels in children diagnosed with ADHD; and (4) it is only through *indirect* evidence that the pharmaceutical companies can make these kinds of statements about chemical imbalances.

In addition, besides the lack of *direct* proof for chemical imbalances, there are significant findings, left unsaid in the advertisements, which contradict the theory. For instance, stimulants will help anyone pay attention, even children who have no diagnosis of ADHD (Rapoport *et al.*, 1978); and the same neurotransmitters, dopamine and norepinephrine, that are implicated in ADHD are implicated in numerous psychiatric conditions.

The issue of altered biochemistry or brain function in ADHD is complex and contested (see chapter four by Leo and Cohen). Consumers reading these advertisements, however, will have no inkling of this fact. They may also lack the skills to digest complex information on neurochemistry, but, in fact, these skills are not necessary to understand the bottom line on biochemistry and ADHD: All behaviour has its basis in neurochemistry, but despite impressive technological advancements and much research, claims of chemical imbalance in ADHD remain unconfirmed hypotheses. Will consumers reading these ads be under this impression?

> *It is a medical condition linked to a chemical imbalance in the brain. It is officially recognized by leading medical experts and institutions, including the US Surgeon General, the American Psychiatric Association, and others* (Strattera.com, 2007).

To add to the confusion, the Strattera™ website intersperses, or 'name drops,' amongst its description of chemical imbalances, the names of official organizations such as the Surgeon General and the American Psychiatric Association. While it is true that both these organizations claim that ADHD is a medical condition, to our knowledge, neither organization has ever provided direct evidence that ADHD is linked to a chemical imbalance or any other biological deficit.

Nature versus nurture

> *ADHD is a physical disorder caused by differences in how the child's brain works. Anxiety-producing factors, such as family conflicts or disruptions, can aggravate the disorder, but they do not cause it* (Ritalinla.com, 2006).

> *The National Institute of Mental Health states that scientists are finding more and more evidence that ADHD does not stem from home environment, but from biological causes* (Strattera.com, 2007).

Contrary to what is implied in these advertisements, the part played by genetics in ADHD – large or small – in no way rules out the possibility of the environment also playing a role. Even those scientists who believe that genes are extremely important will not go so far as to entirely discount the influence of the environment.

For many adherents to the genetic position, the greater concordance rate of ADHD in identical twins compared to non-identical twins is the strongest evidence in support of the genetic position, yet even these adherents acknowledge that this same data also points to an important role for *the environment*. In the words of ADHD genetic researchers Faraone and Biederman:

Most scientists who study the genetics of psychiatric disorders embrace the idea that these disorders are influenced by both genes and environmental factors. In fact the twin studies . . . provide the strongest evidence that environmental risk factors play a substantial role in the etiology of ADHD (Faraone and Biederman, 2000, p. 568).

Faraone and Biederman's explanation about the etiology of ADHD is clearly at odds with that put forth on Strattera™ website, which is in turn credited to the NIMH. Like many psychiatric genetic researchers, Faraone and Biederman are proponents of the diathesis-stress theory, which postulates that some children are born with a genetic predisposition to ADHD but that environmental triggers are necessary for the development of ADHD.

A recent paper in *Biological Psychiatry* highlights the fact that a person's childhood experience may interact to affect his or her risk of developing depression. According to Shelley Taylor, PhD, the lead researcher of the study, 'Genes are not destiny,' and, 'That means, among other things, that there is an important role that parents and even friends can play in providing protection against the risk of

depression that stress can confer' (Taylor *et al.*, 2006; Hitti, 2006). As Shelley shows, contrary to the advertisements, scientists have not ruled out a role for the environment in the development of mental illnesses.

In advertisements for ADHD, the supposed genetic basis for ADHD justifies medical treatment. However, left unsaid in these same advertisements, is that a presumed genetic defect is in no way a prerequisite to prescribing stimulants. As of now, the medical community finds it entirely acceptable to prescribe medication for psychological stress brought on by environmental stressors. One need look no further than foster care programs, which medicate an inordinate number of children. Presumably, the common factor in these children is not their genetic makeup but their common environmental triggers. Although ADHD is considered a genetic defect, looking for a common gene in foster home children to explain their behaviour would seem to be a fruitless effort. Conversely, the results of a survey of environmental stressors in the children's lives would probably be very fruitful. The diagnosis and medication of children in foster homes is perhaps the best example of how, genes and biology aside, it is still an acceptable practice to medicate children whose behaviour is explained by the environment.

Several of the pharmaceutical companies' websites provide a page of questions for patients to print and take to the doctor, yet many of the questions are answered right on the website. On the Ritalinla.com website (http://www.ritalinla.com/info/treatment/ask-your-dr.jsp), the first question parents are to ask their doctor is, 'What are the benefits of Ritalin LA?' The answer provided on the website is, 'The ADHD medication Ritalin LA® (methylphenidate HCl) has been proven in studies to give children with ADHD important benefits such as: . . . ' and the list goes on. Thus, parents arrive for a consultation with their doctor primed not only with a list of questions but also with the preprinted answers downloaded from the pharmaceutical company website. Doctors who give answers different from the script could very likely see their patients go down the street to another doctor.

Adderall™ campaign

In 2005, Shire Pharmaceuticals launched a widespread advertising campaign for their ADHD medication, Adderall XR™ (amphetamine). This campaign included advertisements in popular magazines and took place at a time when Adderall™ was skyrocketing in popularity. At

the conclusion of the print advertising campaign, the following content was found on the AdderallXR.com website. These statements are covered in some detail here because they represent some of the most seductive claims put forth within psychostimulant advertising, and also because this particular campaign is one of the largest thus far. In this campaign, Adderall™ is promoted using the following phrases:

> *'A Trusted Solution for ADHD'* (Print campaign and AdderallXR.com).

There is little doubt that parenting a child diagnosed with ADHD can be exhausting, and most parents will naturally be looking for a 'solution.' However, the word 'solution' would seem to be an exaggeration – not just for Adderall™, but for any pharmacological intervention prescribed to children diagnosed with ADHD. Every scholarly source on ADHD that we are aware of recommends a holistic, multi-factorial approach, including educational interventions, behavioural techniques, family therapy to address long-standing conflicts, and so forth. The evidence-based treatment of ADHD, in fact, recommends using psychotimulant treatment as one modality among many in the integrative, combined treatment of ADHD. In fact, the Adderall™ prescribing information recommends this as well.

Combining the known necessity for multi-modal treatment of ADHD with the fact that many, if not most, children have residual symptoms even while being prescribed psychostimulants raises an important question: In light of these facts, can Adderall™ be accurately characterized as a 'solution' to ADHD? If parents believe these advertisements and approach a physician for this 'solution,' how will they react to a physician who is reluctant to prescribe psychostimulants in their particular case? How will they react to a physician who opines that Adderall™ is not a 'solution,' but simply one potential intervention that may or may not be as valuable as non-pharmacological approaches in a particular case?

> *'Schoolwork that Matches His Intelligence'* (Print campaign and AdderallXR.com).

Many children with ADHD struggle academically, and an improvement in this arena is welcomed by both parents and teachers alike. Psychostimulants are well known to improve concentration, and this effect is not dependent upon a diagnosis of ADHD, but takes place in

'normals' and among those who are above-average achievers in high-demand situations, for instance, among fighter pilots flying extended missions. The claim that Adderall™ will allow a child to complete assigned work at a rate that matches his or her intelligence is seductive, perhaps even more so, because many parents naturally believe that their children are quite intelligent.

However, the veracity of this statement is extremely questionable. There is scant evidence that long-term treatment with amphetamine results in a sustained improvement in global academic performance. A short-term study using a 'classroom analog' found that children who had taken Adderall™ did increase their production at completing math questions over a twelve-hour day, but it is highly questionable whether this one short-term experiment equates to the advertising claim made here. For instance, we have not seen any psychiatric research that establishes, for instance, that children on Adderall™ will manifest academic performance more highly correlated with their IQ than children who are administered a placebo. Such experiments are probably yet to be conducted. We have also not seen any research demonstrating that Adderall™ improves long-term academic performance, as measured by grades – curious, given that this outcome measure is easily obtained. As Furman discusses in chapter two of this book, there is good evidence that stimulant medications do not improve learning *per se*.

> *'Friends that ask him to join the group'* (Print campaign and AdderallXR.com).

All parents want their children to have a happy and enjoyable social life, thus this advertising ploy will ring poignantly for most parents. However, the wording is particularly troubling, as the makers of Adderall™ are literally claiming that prescribing their medication will have predictable, positive effects on the social contacts of those children receiving treatment. We are not aware of any scientific evidence that this is, in fact, true, or any reason why this should be reasonably predicted. The psychology of social networks and child development would seem to suggest that there are a myriad of factors that might account for social relationships among children and that ADHD symptoms are but one facet of a multi-factorial system.

For instance, consider an adolescent child who formerly was impulsive, labeled as a 'weird kid,' and therefore was quite unpopular. Taking stimulants, she becomes less impulsive, but her reputation is already established, and although she is now far less impulsive, her social contacts do not respond to her differently now – she is not asked to 'join the group.' The advertising claim would seem to go unsubstantiated in this theoretical example. Or, consider the child who is popular among other children because he is extroverted and often makes wisecracks in class; upon being prescribed stimulants, he becomes quiet and compliant, but his friends now consider him boring.

This second example is of interest, because Adderall™ is known to cause nervousness, emotional lability, and depression (FDA,2008). Obviously, these symptoms could be harmful to social adjustment. The FDA has raised concerns about the potential for psychostimulants to cause psychotic symptoms, aggression, and suicide. A link between chronic stimulant use and depression is well established. Thus, it seems that Adderall™ is being marketed using the phrase, 'Friends that ask him to join the group,' when, in fact, Adderall™ appears to have the potential to cause psychiatric symptoms that are potentially destructive to the process of social adjustment, at least in some children (FDA, 2008).

A similar claim is that Adderall™ will result in 'Family hour that lasts for hours.' This claim assumes that a very complex system, a family, ostensibly consisting of multiple members and their interactions and collective resentments, appreciations and biases, can expect that family time will be reliably extended by prescription of stimulants to one member, the child. It is subject to the same faulty logic brought up previously.

The Adderall™ webpage also provides a 'Doctor Discussion Guide,' which is a checklist that a parent can fill out online, click 'next,' and then immediately get a report to print and take to the doctor to start off the discussion about ADHD, and presumably about Adderall™. It is hard to imagine a doctor explaining anything about ADHD that does not fit the pharmaceutical companies' agenda, to a parent holding one of these preprinted checklists (Adderall.com).

Information asymmetry in mental health

Information asymmetry (or asymmetrical information) is an economic term referring to a situation wherein one party has more or higher-quality information than the other. The classic example, for which George Akerlof won the Nobel Prize in 2001, is the market for used cars, wherein sellers have intimate knowledge of their vehicles' reliability but buyers face significant uncertainty. This concept of information asymmetry also has applicability to the physician-patient relationship;

physicians have extensive training and knowledge in medicine, while most patients do not. For the manufacturers of psychostimulants and others involved in the 'ADD enterprise,' information asymmetry is a positive thing. It is in their financial interests for patients to be under the impression that ADHD is an uncontroversial, scientifically-established biologically-based genetic brain disease best treated with stimulants. As this analysis has demonstrated, this understanding represents a significant level of information asymmetry as compared to the overall scientific literature.

If DTCA were the only source of information about ADHD and psychostimulants, this would represent a very high rate of information asymmetry indeed. However, this is not the case. There are many other sources of information on these topics, among them two major institutions that may stand as a buffer to the consumer advertisements. These are (1) the press, serving a watchdog function for the public good, and (2) the academic medical journals, traditionally thought of as the guardians of evidence-based medicine. Taken together, these two institutions certainly have the potential to level the playing field and reduce information asymmetry of the type that is found within DTCA.

Academic medicine and DTCA

Whether it will be different in Britain remains to be seen, but in America, concurrent with the growth of consumer advertising has been a weakening of the wall between academic medicine and the pharmaceutical companies. According to Arnold Relman, a past editor of the *New England Journal of Medicine*, 'The academic institutions of this country are allowing themselves to be paid agents of the pharmaceutical industry. I think it's disgraceful' (cited in Moynihan, 2003, p. 1190). In a provocative essay in the *Public Library of Science Medicine*, Richard Smith, past editor of the *British Medical Journal,* boldly stated: 'Medical journals are an extension of the marketing arm of pharmaceutical companies' (Smith, 2005, p. 364). What Smith and Relman understand, and what the press has not focused on, is that the problem is not just with the companies but is also with scientific papers (Smith, 2006). The pharmaceutical companies make an easy target, but they have not operated alone.

Fortunately, their British counterparts may not show the same willingness to help the pharmaceutical companies. In general, the British medical journals have shown a greater willingness to publish papers

written by scientists who take a critical view of the evidence base. Whether they can maintain this practice once the consumer advertisements become legal remains to be seen. Should the British press buckle under the pressure, the loss of its cautionary voice could have a negative impact on psychiatric science worldwide. Take the studies of SSRIs in children: While the American journals were publishing selective data, released by the pharmaceutical companies, about the use of SSRIs in children, in Britain, the *British Medical Journal* and *The Lancet,* both more open to non-industry views, published papers examining the unpublished data. It was these papers, published in the British journals, which provided the impetus for the FDA to step into the fray and look more closely at the original trials, and to eventually issue a black box warning for the SSRIs. Moreover, *The Lancet* editors characterized the studies as, 'Confusion, manipulation and institutional failure' (Editors, 2004, p. 1335). David Healy has gone so far as to suggest that these studies highlight the need for a new category of journal articles as the papers were conceived primarily as marketing projects and not scientific endeavors (Healy, 2003).

Much of the general public would be amazed to know that, though a university professor may be listed as an author on a scientific paper, it in no way guarantees that the professor actually wrote the paper. In some cases, scientific papers are written by a company representative, and the company then pays a professor for the use of his or her name on the author list. The practice is known as ghostwriting and is becoming more common in academic medicine. In 1998, the *Journal of the American Medical Association* (JAMA) published a survey documenting that eleven percent of the articles published in top-tier American journals had been ghostwritten (Flanagin *et al.*, 1998). In 2002, the *New York Times* published an article about the creation of a ghost-written article as part of the marketing campaign for a new long-acting version of Ritalin™ (Ritalin LA™), which acts for eight to nine hours, versus the competitor's twelve-hour version. According to the *Times*, the problem for Novartis, the manufacturer, was that it had no scientific evidence to back up claims that Ritalin LA™ was better. So Novartis hired Intramed, a medical education company, which in turn commissioned two university professors to write an article emphasizing the benefits of Ritalin™ LA. The two professors both agreed, and, according to the *Times*, in a tape-recorded conversation between the doctors and Novartis, one of the doctors said, 'I think we're quite clear on what you want the next manuscript to

look like' (Petersen, 2002). To help with the article, Intramed also hired a ghostwriter, Linda Logberg, to write the first draft for the two doctors. Neither of the two doctors, Novartis, or Intramed saw any problem with the practice, however the ghostwriter saw the whole process as marketing masquerading as science. When the *Times* piece was published, the ghost-written article had not yet been published. The fate of the ghost-written article in question remains unknown, but a Pubmed search reveals that they were coauthors of a review published in 2003 on the pharmacotherapy of ADHD medications, with a focus on the long-acting versions of methylphenidate (Markowitz *et al.*, 2003).

In a recent interview, William Pelham provides insight into the interplay between the pharmaceutical companies, the medical journals, and academicians (Hearn, 2004). On the webpage of the ALZA Corporation, a subsidiary of McNeil Pharmaceuticals (*Concerta.net*), there are statements praising the benefits of Concerta, one being that ninety-six percent of the children taking the drug do not experience significant side effects (appetite, growth, and sleep). Pelham's study is cited as supporting evidence for this claim (Pelham *et al.*, 2001). However, in his interview, Pelham expressed dismay about the way his study was being characterized on the website, because his study was limited to children who had already used Concerta with no significant side effects – children who exhibited side effects would not have been placed in the study to begin with. Thus, the experimental design of the study included a pre-study phase to virtually guarantee that the children in the study would not exhibit side effects. Pelham expressed astonishment over the fact the FDA allowed ALZA to use his study to make its claims.

In addition, Pelham mentions that the company wanted him to delete a paragraph he wrote about the importance of behavioural therapy. In his words: 'The people at Alza clearly pushed me to delete a paragraph in the article where I was saying it was important to do combined treatments (medication and behavioral)', and 'It was intimidating to be one researcher and have all these people pushing me to change the text'.

For a follow-up paper, Pelham also mentions that the company did the data analysis and coordinated the writing of the paper. In his words, 'I insisted on seeing the analyses and having major inputs into the manuscript, and it was like pulling teeth to get wording and analyses changed. It was like a whitewash – a praise to Concerta' (Hearn, 2004).

The media and the pharmaceutical companies

Unknown, and unquantifiable, is the effect of DTCA on the interactions between the pharmaceutical companies and the press. In the US, the pharmaceutical companies spend approximately $4 billion a year on advertisements; in 2004, the combined DTCA revenue for the *New York Times, Time,* and *Newsweek* was $123 million (Lieberman, 2005). Whether the press can maintain its objective status when it comes to reporting on the pharmaceutical companies, at the same time it is receiving large amounts of money from the companies, is debatable. In 2003, *Time* published the article, 'Medicating Young Minds,' about the increasing use of psychotropic medications for young children (Kluger, 2003). The article had this somewhat surprising statement about the use of SSRIs in children: 'While an earlier generation of antidepressants – tricyclics, such as Tofranil – didn't work in kids, SSRIs do' (Kluger, 2003). That statement is surprising because, at the time it was made, the evidence base for using SSRIs in children was marginal – at best. And it was certainly no secret that it was marginal, as there were numerous scientists and physicians pointing out the problems with the studies of SSRIs in children. Even officials at the FDA had acknowledged earlier in the year that the evidence base for the use of these medications was slim and the only medication to show superiority over placebo was Prozac. In their words: 'for the 7 drugs evaluated in paediatric major depressive disorder (MDD), data reviewed by FDA were adequate to establish effectiveness in MDD for only one of these drugs, Prozac (fluoxetine)' (FDA, 2003). How the reporters and, more importantly, the editors at *Time* became so convinced about the effectiveness of the SSRIs in children is unclear, but it was clearly *not* by reading the scientific literature. Take Prozac, which was the only one of the eight SSRIs that the FDA approved for children. It was approved by the FDA for children in 2003, the same year the *Time* piece was published, on the basis of just two controlled clinical trials. In the first study, Prozac barely beat out the placebo, and in the second study, sixty-five percent of the children in the Prozac study had a beneficial response, compared to fifty-three percent of the placebo patients, a difference that was not statistically significant (see Leo, 2006, for a more extensive discussion). In fact, just two months after *Time's* declaration that the SSRIs work in children, the editors changed their minds and published another article titled, 'Prescription for Suicide?' This second article was much more circumspect about the effectiveness of the SSRIs in children

'most studies on effectiveness aren't really definitive. They don't prove one way or the other whether the drugs work significantly better than placebos' (Lemonick, 2004). As exemplified by the above example, it is too easy for the media, just as it is for the consumers, the journal editors, and physicians, to get caught up in the whole marketing blitz.

One of the more egregious practices, highlighting the influence the companies have over the press, is that television stations now present short clips, called video news releases, or VNRs for short, as if they were prepared by reporters when they were actually prepared by a corporation. The viewers believe they are watching an unbiased news presentation, when they are really watching an infomercial produced by a business. Instead of acting as a watchdog, the press is reduced to nothing more than a mouthpiece for the company. While not as egregious, another unsettling practice concerns reporters failing to maintain a critical viewpoint when hearing from 'health care experts.' As an example, take the recent three part series in the *New York Times* on children and mental health. Part three of the series focused on the issue of polypharmacy for children and correctly pointed out there is no solid evidence for giving multiple psychiatric medications to children. True, but hardly earthshaking, and few people will defend – at least publicly – the practice of giving multiple psychotropic drugs to children, some as young as twelve months old. Yet, while openly critical of polypharmacy for its lack of evidence, the *New York Times* gives its stamp of approval to the practice of giving single medications to children, although the evidence base appears to be no better than that for polypharmacy. 'Meager' best describes the strongest evidence the *New York Times* can scrape together: 'There is little doubt that some psychiatric medicines, taken by themselves, work well in children. For example, dozens of studies have shown that stimulants improve attentiveness.' Hardly a ringing endorsement for the practice. Can this well-known fact, that stimulants improve attention span, seriously be considered as valid evidence in support of using antipsychotics or antidepressants in three-year-olds? For that is the subject of the *New York Times* article in the first place. Hard to imagine – and it is even harder to imagine that the editors at the *Times* did not question their own flimsy evidence in making this statement.

Taking this train of thought a bit further, what about coffee and cocaine? They are also stimulants and improve attention span; do their effects also count as evidence in support of diagnosing and treating three-year-olds with psychiatric medications?

Given these examples, it is difficult to characterize the mainstream press as acting in an aggressive 'watchdog' role when it comes to pharmaceutical companies, children, and psychiatric medications.

The harmful effects of Ritalin™ turned upside down by the popular press

Imagine the following straightforward experiment, which has been performed numerous times with various drugs. Researchers administer a certain drug to young rats, and subsequently find that the drug has harmful long-term effects. If the drug in question is illicit, the results are usually held up as one more reason to refrain from using the drug. If the drug happens to be a prescription drug, most scientists would at least *suggest* the need for increased caution by the medical profession – especially if the drug's target market is young children.

Interestingly, William Carlezon and his colleagues at Harvard Medical School recently conducted the above experiment with Ritalin™ (Carlezon, Mague and Anderson, 2003), and, indeed, the researchers discovered that Ritalin™ had harmful long-term effects on the brain of developing rats. In their study, young rats exposed to Ritalin™ had an increased risk for depression later in adulthood. You would think that this would *suggest* that children diagnosed with ADHD and given Ritalin™ *might* be at risk. Instead, the popular press reported that the main message of the study was that children need an accurate diagnosis of ADHD.

Following the publication of the study, the American College of Neuropsychopharmacology (ACNP) published a press release (Lobliner, 2004), which declared that the study only has implications for 'normal' children and not for children diagnosed with ADHD. In fact, not only did the ACNP forgo the slightest suggestion that Ritalin™ *might* be harmful for 'ADHD' children, it went out of its way to explain that the results do not apply to 'ADHD' children. According to their logic, only if you have an *incorrect* diagnosis of 'ADHD' will Ritalin™ be harmful. The press release took data showing that Ritalin™ harms the brains of rats, and turned that data into the message that Ritalin™ will only harm children with an incorrect diagnosis.

The major flaw in the logic starts with the explanation that the rats in the study were not 'ADHD' rats, but were 'normal' rats. Labeling the *rats* as normal allowed the ACNP to assert that the findings only had implications for normal *children*. The ACNP established a

dual role for Ritalin: On one hand, Ritalin™ is beneficial for children diagnosed with ADHD; yet, on the other hand, it is harmful to 'normal' children. When one considers that even drawing a line between 'ADHD' and 'normal' varies widely from one doctor's office to another, from one state to another, or from one country to another, the idea that there is some scientific reasoning involved in where to draw this line lacks credibility. If a committee ever developed a universal standard for ADHD, would Ritalin's™ apparent dual action – beneficial to some, but harmful to others – fall in line with the committee's decision?

A related question comes to mind: if Ritalin™ only produces harmful effects on the 'normal' brain, then whose definition of 'normal' will Ritalin™ follow? Many children in other parts of the world would not be given a diagnosis of ADHD in their own countries, but in America they would be easily labeled with ADHD. A correct diagnosis in America might not be the same as a correct diagnosis in their home country. Would Ritalin's™ effect on the brain follow their home countries' definition of ADHD or America's definition? As pointed out earlier in this paper, different medical organizations follow different criteria for the diagnosis of ADHD, which leads to dramatically different prescription rates.

As an example of the problem with the ACNP's logic, imagine these two scenarios. The parents of a young teenage boy are concerned about his grades and take the boy to a psychiatrist. After completing a short questionnaire, the boy is diagnosed with ADHD and given a prescription for Ritalin™. According to the ACNP, for this boy, the Ritalin™ will have a beneficial effect. Another boy, a classmate of the first boy, has a week of exams coming up and wants to improve his grades, so he decides to buy some Ritalin™ from the first boy. According to the ACNP, Ritalin™ will harm this boy. The idea that Ritalin™ is *not* harmful to the boy whose parent's filled out a short checklist, but is harmful to the boy who bypassed the checklist is problematic.

One month later, working from the original ACNP press release or one little changed from the original, the *Wall Street Journal* uncritically reported the ACNP's version of the study, 'This latest research has particular significance for healthy children who have been wrongly diagnosed and put on ADHD medication' (Parker-Pope, 2005). But the *Wall Street Journal* has missed the fact that there is no good reason to limit the significance of this study to *misdiagnosed* children. Indeed, this research has particular significance for *all children* taking Ritalin™, whether it was prescribed by a doctor or not. In the animal

world there is no line between 'normal' and 'ADHD,' and there is no reason for the ACNP or the *Wall Street Journal* to draw one.

Misdiagnosed ADHD?

Some in the media have pejoratively referred to the practice of using a medication to improve performance in the classroom as 'academic doping.' What the press does not seem to understand is that 'academic doping' is fully supported by the medical community – as long as the medication is provided by a doctor. News organizations often present the controversy surrounding the increased use of Ritalin™ as if there were a clear boundary between the two situations – on the one side, Ritalin™ being used to *appropriately* treat a 'medical' illness, and on the other, Ritalin™ being used *inappropriately* to improve academic performance. A recent Reuters news report commented on the matter as follows:

> Results of a survey of physicians suggest that parents often request a 'behavioural drug,' such as Ritalin™, with the goal of enhancing their child's academic performance *rather than treating an illness*. (Gale, 2006, Italics added).

Or take a recent editorial in the *Washington Post* titled, 'Millions Have Misused ADHD Stimulant Drugs, Study Says,' in which the author states, 'The statistics are striking because many young people recreationally using these drugs are seeking to boost academic and professional performance, doctors say' (Vendantam, 2006). In these examples, the assumption by the press is that using Ritalin™ to improve grades is a 'misuse' of the drug. Yet the practice of prescribing stimulants to improve academic performance is exactly why these medications are used in the first place, and the practice is fully sanctioned by the medical community. In fact, no official medical organization that supports the use of Ritalin™ has ever said that using Ritalin™ to improve academic performance is inappropriate.

According to Dr. Joseph Biederman, a leader in the child psychiatry profession, 'If a child is brilliant but is doing just OK in school, that child may need treatment, which would result in their performing brilliantly at school' (Gale, 2006). Sharing Biederman's view, as we have shown in this paper are the pharmaceutical companies who advertise improved academic performance as one of the features of stimulant medication. Consider the recent advertisement for Daytrana™, a Ritalin™ patch, manufactured by Shire, and applied to the hip in the morning: 'When you apply the Daytrana™ patch,

you can help your child get ready for school, homework, and his entire day.'

Even the patient support groups condone the use of Ritalin™ for academic enhancement. Take the recent example of Johnny Holliday, a celebrity who is a spokesman for Children and Adults with ADHD (CHADD). In *Selling Sickness*, by Moynihan and Cassels, they report on the following interview with Holliday at a CHADD golf benefit:

Holliday said he was happy to help out with the event for free, because his daughter had once suffered with ADD, discovered in her case in eighth grade. 'I know the frustration she went through and her parents went through,' he told a reporter from the BMJ. As for the drugs, Holliday said, she had only taken her medication intermittently during school time, mainly to help with tests. 'It really did the job,' he said, before jumping back into his golf cart and adding with fatherly pride that she had just graduated from college with honors (Moynihan and Cassels, 2005, p. 63).

Holliday is not alone in his enthusiasm for the attention-enhancing aspect of stimulants, as a recent survey of physicians reported that two-thirds of primary care doctors recently reported receiving requests from parents to prescribe drugs with the goal of enhancing their child's academic performance (Gale, 2006).

In 1999, the editors of the journal, *Pediatrics,* elicited commentaries from several prominent physicians about the case of a teenage boy who had been taking Ritalin™ for several years. The editors saw the boy's scenario as an interesting case, worthy of commentary from a group of prominent child psychiatrists (Stein *et al.*, 2001; Cohen and Leo, 2002). Paradoxically, they have provided a much more interesting, albeit unintended case study. From a sociological point of view the subject of the case is not the boy, but is, instead, the doctors and journal editors, In other words, the behaviour of the adults is of much more interest than that of the boy. The case provides an excellent example of: (1) how there is little science involved in the diagnosis of ADHD; (2) how the medical community fully supports the use of stimulant medication as a performance enhancing drug; (3) how the same mindset that approves of using one psychotropic drug easily leads to the use of multiple medications; and (4) how the mainstream medical journals have given little attention to the ethical implications of controlling and altering children to meet the demands of our contemporary educational/cultural system.

The fifteen-year-old boy announced to his parents and his paediatrician that he wanted to stop taking his medication:

'I don't need it... I'm fine... I don't see why I should take it.' He purposefully did not take the medication for a few weeks and he said he could not tell the difference... However, his parents observed that his test results, when off the medication, were below his standard scores... They also noted that he was more distractible and less attentive when doing his homework during that time (Stein *et al.*, 2001, p. 974).

The most important variable in determining whether this boy should keep taking his medication was the parental satisfaction with the medication, and the subsequent commentaries all focused on how to convince the boy to continue taking his medication. The boy's wishes were not something to be listened to, but rather something to be managed, whether through dialogue or with another medication. Amazingly, as an example of polypharmaceuticals for children, one of the commentators even suggested that the boy's reluctance to keep taking his Ritalin™ suggested this was a sign that he needed another medication. Thus, the boy, who wants go off his one medication, would instead get two medications. None of the commentators in the *Pediatrics* article conjectured that the boy's wishes might be legitimate. More importantly, as a sign of how one sided the issue has become in the medical community, *the editors* did not give space to a single commentator who questioned the ethics of giving a medication to improve grades.

The ethical questions surrounding the use of Ritalin™ are becoming a larger issue, as once-medicated children are now reaching adulthood. According to a recent survey in the *LA Times*, a significant number of these adults are deciding to discontinue their medication (Healy, 2006b). The *Times* article quotes a twenty-seven-year-old woman who reflects back on the years she was medicated, 'It was kind of weirdly amazing... You get excited about monotonous work, honestly. Like, translating Spanish becomes totally fun... The thing is, it works. But why are we forcing people to be in that position that they should like something that they wouldn't ordinarily' (Healy, 2006a). In just three short sentences, this young woman goes right to the heart of the ethical dilemma of stimulant medication: Is it right to medicate people so that they do well in school? Yet nothing close to her straightforward insight can be found in the entire *Pediatrics* case study, which supposedly included the collective wisdom of an editorial staff, prominent physicians, and academic psychiatrists. The *Pediatrics* case demonstrates that all the talk of genetics, biology, and medicine simply provides a false air of legitimacy to what

is nothing more than the disbursement of a performance-enhancing drug.

As often happens after statistics documenting the increasing use of stimulants for younger and younger children make the headlines, many of the opinion leaders in the psychiatry community state that there is a problem with 'over-prescribing' or 'misdiagnosis,' yet none of these leaders, or any of the major psychiatric organizations, have issued guidelines on how to identify this large group of 'misdiagnosed' children, nor have they clarified what they consider to be improper uses of prescribed stimulant medication (Johnson, 2006; Nakamura, 2002).

The dilemma for medical professionals who want to go beyond simply talking about misdiagnosed children and to actually move on to identifying these children is that, without an objective biological marker demarcating the line between the 'correctly' and 'incorrectly' diagnosed, the sole criterion for determining the appropriateness of stimulant treatment comes down to: are the adults in the child's life satisfied with the medication's effect? Presumably there are not many parents, unhappy with the medication's effects, who still continue to medicate their children. None of the medical professionals who talk about misdiagnosis have ever elaborated on how they plan to tell all these parents of misdiagnosed children that they should not be medicating their children, even though the medication is doing exactly what the advertisements say it should be doing.

Conclusion

In their advertisements, the pharmaceutical companies have intermingled non-controversial statements about the universal effect of stimulants on attention span, along with highly controversial statements about the speculative theory that up to twenty percent of the children in the US have an organic brain disease (NIHCM Foundation, 2005). As we have documented, the claims made in the consumer advertisements of ADHD medications are oversimplified, one-sided presentations of complex medical and social issues. The major difference between the advertisements and the medical literature is that the advertisements portray these issues as having clear, straightforward answers, while the medical literature is filled with ambiguity, conflicting results, and an ongoing debate. The advertising claims we have illustrated are controversial from a scientific standpoint, and at best, most of them should be explained as tentative hypotheses, not well established facts. However, the degree to which this

advertising is shaping the public's perceptions of the issues should not be underestimated.

The full impact that the consumer advertisements have had on the diagnosis and treatment of ADHD requires further study, especially given that consumers may seek out information from other sources, such as the Internet. At present, it appears that information asymmetry is the norm within the ADHD field. There is a critical literature on ADHD, but it is rarely seen from major media outlets or in high-profile mainstream journal publications.

For those interested in providing consumers with well-balanced, scientifically-based information on ADHD, these consumer advertisements are troubling. We hypothesize that they are very effective at achieving their intended effect: guiding patients into the doctor's office and then guiding the conversation with the doctor. We assume that DTCA is an incredibly useful tool for pharmaceutical companies that manufacture psychostimulants. The net effect on the public, and the children who end up taking ADHD medications, is likely to be negative.

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Chapter 11

The Deficiencies of Drug Treatment Research: The Case of Strattera™

David Cohen, Shannon Hughes and David J. Jacobs

By the start of the 21st century, a certain naiveté about the validity of findings from drug industry funded clinical trials seemed to have dissipated from the fields of psychiatry and psychopharmacology. Indeed, only at his or her own risk and peril, and that of his or her patients, would a clinician choose to accept as valid the latest positive findings from the latest clinical trial about the latest 'promising' drug. Even among mainstream observers, there occurred a growing realization that the drug industry had penetrated every nook and cranny of the enterprise of testing drugs for human consumption, and, with the sole aim of increasing market shares for its products and profits for its shareholders, had passed off countless infomercials as scientific studies attesting to the safety and efficacy of these products. A flood of studies, media investigations, actions by regulatory bodies, and leaks from judicial cases documented how the industry had bought off or co-opted presumably impartial academic researchers, journal editors, peer-reviewers, journalists, state health administrators, and federal regulating agencies. Editorials appearing in the most prominent medical journals lamented that the entire clinical trial enterprise might be characterized by deception and manipulation, such that the boundary between marketing and scientific activities had been virtually eliminated.

This chapter explores the extent to which the new critical awareness, as well as parallel regulatory requirements, may have impacted

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The diagnosis of ADHD (attention deficit hyperactivity disorder) has reached epidemic proportions across many countries, having a large impact on how childhood is conceived and understood. Despite this growth, fundamental questions about the nature and meaning of ADHD remain.

Rethinking ADHD brings together a series of international critical perspectives focussing on a variety of issues including genetics, drug companies, nutrition, and culture. The authors invite readers to rethink common assumptions about ADHD, as well as encouraging students, practitioners and parents to question their understanding of the condition and its role in society.

'This is an interesting and challenging book which argues against the common "medical model" of ADHD. The book provides a thorough discussion of the role of different environments and cultures in ADHD, topics which are often underplayed.' – **Dr Julia Carroll**, Warwick University, UK

'This book provides a fascinating overview of the current epidemic of ADHD. By critically analysing the scientific evidence, and exploring the variations in diagnosis between countries, cultures, gender and class it exposes the inadequacy of the concept of ADHD and points towards less toxic ways to help children with behavioural problems.'
– **Dr Joanna Moncrieff**, *University College London, UK*

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ADHD

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RETHINKING ADHD

from brain to culture