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DATABASES

Entrez Gene:
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene
DRD1 | *DRD2*

FURTHER INFORMATION

Tomáš Paus's homepage:
http://brainbody.nottingham.ac.uk/people/paus.php
Matcheri Keshavan's homepage:
http://brain.wayne.edu/kesh/kesh.htm
Jay Giedd's homepage:
http://intramural.nimh.nih.gov/research/pi/pi_giedd_j.html

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SCIENCE AND SOCIETY

Beyond polemics: science and ethics of ADHD

Ilina Singh

Abstract | What is attention-deficit hyperactivity disorder (ADHD)? Why are so many children being diagnosed with ADHD and prescribed medication? Are stimulant drugs an effective and safe treatment strategy? This article explores the current state of scientific research into ADHD and the key social and ethical concerns that are emerging from the sharp rise in the number of diagnoses and the use of stimulant drug treatments in children. Collaborations among scientists, social scientists and ethicists are likely to be the most promising route to understanding what ADHD is and what stimulant drugs do.

Attention-deficit hyperactivity disorder (ADHD) is one of the most common childhood psychiatric disorders in the world[1]. Its core symptoms are inattention, hyperactivity and impulsiveness. Most children are first diagnosed with ADHD when they reach school age[2] and approximately 75% of those diagnosed are male[3]. The most common forms of treatment for ADHD are the stimulants methylphenidate and amphetamine[4].

Rising rates of ADHD diagnosis and stimulant drug use in children have led to a public debate over the validity of the diagnosis, the root causes of ADHD and the ethics of treating children with psychotropic drugs. There are three partially overlapping positions in the debate. First, that ADHD is primarily caused by a combination of biological factors. From this perspective, diagnosis is valid and drug treatment is justified because it corrects an underlying neurochemical imbalance that affects cognitive and motor functions. Second, that ADHD is caused by a combination of biological and social factors; the diagnosis does not yet adequately capture the heterogeneity and complexity of the disorder. This perspective accepts the utility of stimulant drug medication, but some

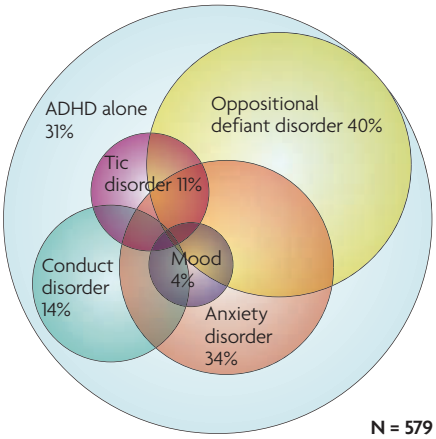


Figure 1 | **Co-occurring disorders in the Multimodal Treatment Study of children with ADHD.** Participants in the National Institute of Mental Health Multimodal Treatment Study for attention-deficit hyperactivity disorder (ADHD) reflect the complex mental-health profiles of US children with ADHD. Only a third of the children in the study had a diagnosis of ADHD alone. More than half of the children had conduct or oppositional defiant diagnoses in addition to having ADHD, and a significant proportion of those with conduct and oppositional diagnoses also had an anxiety disorder. Figure modified, with permission, from REF. 18 © (2001) Lippincott Williams & Wilkins.

proponents are sceptical of the widespread use of psychotropic drug treatments over other interventions, such as behavioural therapies[5]. Third, that ADHD is a valid disorder but its primary causes are environmental (for example, maternal smoking, lead exposure, food additives and so on)[6–8]. This perspective views early recognition, prevention of exposure, and raising awareness about predisposing environmental factors as ways to reduce dependence on stimulant medications[9]. Any one of these positions involves a variety of stakeholders: parents, teachers, clinicians, scientists, regulators, social scientists, ethicists and children themselves. There is a fourth position, which is sceptical that ADHD is a real disorder. This position is sometimes identified with scientologists, but it is also represented by a separate, and more thoughtful, sociological critique[10,11].

In the past decade, scientific research has focused on strengthening the first position, with an emphasis on identifying primary genetic causes of ADHD[4]. More-recent evidence, however, suggests that complex psychiatric disorders are mediated by a combination of genetic and environmental factors[4,12,13]. Scientific research into the complex and potentially multiple aetiologies of ADHD is still in early stages[14]; however, it is attracting a lot of attention as ADHD becomes a global phenomenon: in the past decade rates of diagnosis have increased sharply in most countries around the world[15]. These increases are linked to parallel growth in the consumption of stimulant medications[16]. A better scientific understanding of the aetiology of ADHD might clarify whether the growing number of school-age children that are being diagnosed with ADHD and taking stimulant drugs represents over-diagnosis and overuse of stimulant treatments or an actual increase in ADHD prevalence[4,17].

Growing scientific evidence suggests that ADHD cannot be explained by genetic or environmental factors alone. Research that integrates social and scientific perspectives is likely to achieve a more complete explanation. This article reviews the scientific and social debates over ADHD and identifies key areas in which social investigations should be integrated with scientific research to generate richer models of the causes of ADHD and better understanding of the validity of the diagnosis. The ethics of ADHD diagnosis in children are also discussed, in order to outline areas in which ethical analysis can contribute to an understanding of the relative risks and benefits of ADHD diagnosis and treatment approaches.

ADHD diagnosis

ADHD is characterized by a cluster of behavioural symptoms that are considered separate from, but highly correlated with, other childhood psychiatric conditions, such as conduct disorder and oppositional defiant disorder[18]. The relationship between high levels of co-morbidity (FIG. 1) and underlying genetic factors is unclear[12].

Two definitions are currently used in the diagnosis of ADHD. American psychiatrists follow the ADHD diagnosis described in the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV)[19]. DSM-IV describes two primary categories of behavioural symptoms: inattention and impulsivity–hyperactivity; and three subtypes of ADHD: inattentive type, hyperactive–impulsive type, and combined. The World Health Organization's manual, the *International Classification of Diseases, 10th edition* (ICD-10) calls the condition Hyperkinetic Disorder (HKD or HD)[20]. ADHD and HD symptoms are very similar; however, ICD-10 requires all three symptoms — hyperactivity, inattention and impulsivity — to be present for a diagnosis to be made.

A full diagnostic assessment for ADHD should include an evaluation of the symptoms' pervasiveness, duration, resultant impairment and age of onset. Studies have found that a diagnosis of ADHD is 3–4 times more likely if DSM-IV criteria are used than if ICD-10 criteria are used[21,22]. This is thought to be due to the emphasis on impairment in the ICD-10 diagnosis, the fact that ICD-10 requires more symptoms of the disorder to be more pervasively present and the fact that ICD-10 does not allow HKD to be co-morbid with other child psychiatric diagnoses[23,24].

Although both the ICD-10 and the DSM-IV diagnoses are reliable[25], neither DSM-IV nor ICD-10 captures the phenotypic heterogeneity that is seen in clinical contexts where ADHD is diagnosed. This is because both manuals use a categorical, rather than a dimensional, system of classifying symptoms and making a diagnosis[12]. Categorical diagnosis requires a hard distinction between normal and pathological symptoms. This is in contrast to classifying symptoms along a continuum, or a dimensional spectrum, from normal to dysfunctional. Both manuals are currently under review and new editions will emerge in the next few years. There is much discussion over the possibility of moving from categorical to dimensional diagnoses in the next DSM[26].

In addition to the complex descriptions that are used to classify ADHD behaviours, there are different methods for diagnosing ADHD, especially in the United States[27]. These range from child behaviour checklists that elicit information from multiple sources (such as the Connors Parent/Teacher Rating Scales) to parent interviews[28]. In the United States, the mental-health-related expertise of the diagnosing clinician can vary considerably (it is possible to obtain a diagnosis of ADHD from primary-care physicians (general practitioners), nurses, paediatricians, psychiatrists and neurologists[28]), whereas in most of Europe, initial evaluations for ADHD are usually performed in a specialist child-psychiatric service.

ADHD prevalence

Given the differences in diagnosing ADHD described above, it is not surprising that ADHD prevalence rates vary widely both within and across countries. A recent meta-analysis of ADHD prevalence rates by geographic region suggests that South American countries have the highest prevalence (11.8% of school-age children) and European countries have the lowest prevalence (4.6%)[23]. Within-country estimates, based on individual studies, show even greater variation:

US prevalence estimates vary from 2% to 18% of school-age children[19]; UK prevalence estimates vary from 0.5% to 26% of school-age children[29–32]. These variations could be due to the use of different sources of evidence — for example, diagnosis of a random sample of school-age children or a survey of paediatricians — which complicates a direct comparison of the estimates.

More reliable information is available on national and international increases in ADHD diagnoses. These figures are extrapolated from the growth in international use of stimulant drugs — which are used almost exclusively to treat ADHD (FIG. 2). Economists have found that in the past decade, increases in the use of ADHD medications in non-US OECD (Organization for Economic Cooperation and Development) countries have surpassed rates of increase in the United States[15]. The United States still spends more money than all other countries — 83% of the global market share — on ADHD medications, but rates of increase in US spending on ADHD medications can be explained by the shift to more-expensive, long-acting formulations such as Concerta (Alza Corporation)[15]. In developing-world nations, increases in annual use and spending on ADHD medications are greater than 20%[15]. Thus, as some economists have stated, "understanding determinants of use of ADHD medications, and their costs, and their potential risks and benefits, is now a global issue" (REF. 15).

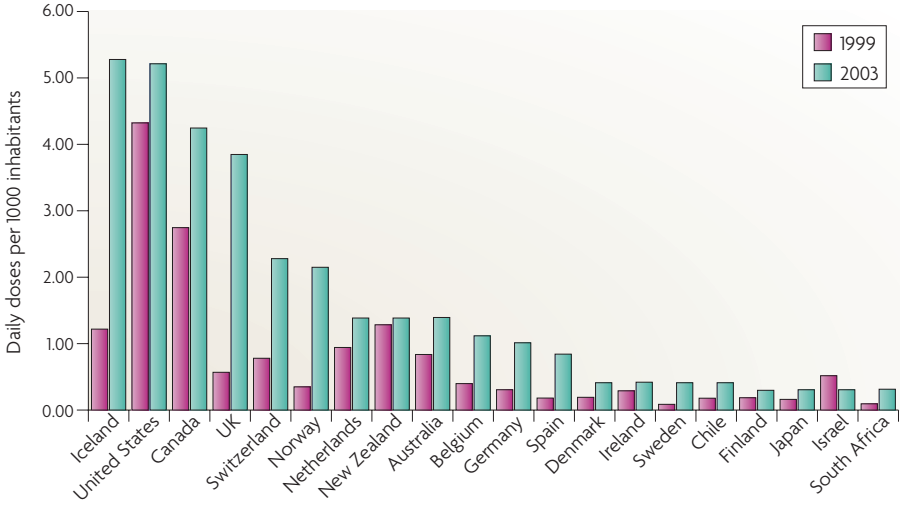


Figure 2 | **Worldwide consumption of methylphenidate.** In 2003, Iceland and the United States had the highest per capita consumption of methylphenidate in the world. Growth in consumption between 1999 and 2003 was highest in European countries. The only country in which methylphenidate consumption decreased during this period was Israel. Figure reproduced, with permission, from REF. 115 © (2005) International Narcotics Board.

State of the science of ADHD

The social, clinical and behavioural complexities of ADHD create enormous challenges for scientific research. Rather than looking for discrete causal factors in ADHD, investigations are increasingly focused on identifying complex developmental pathways that link genetic, biological and environmental risk factors to phenotypic expression in multiple different combinations[33–35].

Genetic factors in ADHD. Genome-wide association studies have been largely inconclusive, although one study has found weak associations between variants of the dopamine transporter (DAT) and the dopamine receptor DRD4 and ADHD[36]. Although these findings have been replicated for several genes, overall results are variable and reported effect sizes are small[37]. Variations in the serotonin transporter gene have also been implicated in susceptibility to ADHD, although the role of serotonin in ADHD is not well understood[38].

The variability in findings and lack of replication is presumed to be due at least in part to diagnostic heterogeneity. To address this problem, researchers have begun to target measurable intermediary neurobiological components (endophenotypes), such as the dopamine system[39]. The goal of identifying valid endophenotypes is to increase the power of genetic research to determine susceptibility genes for ADHD[12]. When integrated into complex models of neurodevelopmental pathways associated with ADHD, genetic risks for ADHD could theoretically inform ADHD diagnosis and contribute to improved treatment algorithms[33].

Neurobiology of ADHD. The well-established dopamine theory of ADHD suggests that dysfunctions in the dopamine neurotransmitter system interfere with proper functioning in key neuropsychologic domains, such as attention and motivation[4,33]. Thus, putative neuropsychological endophenotypes are largely focused on executive-function deficits that involve the dopamine system[35]. It is unlikely, however, that executive-function deficits are necessary or sufficient for expression of the disorder[14,40], and it is unlikely that the dopamine system is uniquely implicated in ADHD[41]. Studies in animal models have shown that the neuroadrenergic and serotonergic neurotransmitter systems are also affected by stimulant drug treatments[42]. Animal models also confirm the heterogeneous origins of ADHD, as animals with substantively different neural defects model the behavioural symptoms of ADHD[42]. Eventually, neuropsychologic heterogeneity is expected to identify distinct subtypes of ADHD, which could shift diagnostic attention from symptoms to neurocognitive factors[33].

Neuroimaging findings in ADHD. A network of distributed brain regions is thought to be involved in attention, cognition and behavioural self-regulation[43]. Indeed, structural neuroimaging studies in ADHD research suggest that patients have widespread anatomical differences from controls; smaller volumes in the dorsolateral prefrontal cortex, the caudate nucleus, the corpus callosum and the cerebellum have been reported[44]. Functional neuroimaging studies predominantly using positron emission tomography (PET) and functional MRI (fMRI) support the involvement of frontostriatal abnormalities (particularly in the dorsal anterior cingulate cortex, the lateral prefrontal cortex and the striatum) in ADHD[45]. The study of neurobiological endophenotypes in ADHD has led to a better understanding of the relationship between structural and functional abnormalities in ADHD. Dopamine deficits are thought to have a role in the anatomical and functional differences observed in dopamine-related brain areas, including the caudate nucleus, the globus pallidus, the corpus callosum and the cerebellum vermis[46].

Volumetric and anatomical differences in brain areas are integral to comprehensive models of ADHD pathophysiology, and they could theoretically be used to inform

neuroimaging biomarkers of ADHD. Such biomarkers could eventually become part of a comprehensive clinical evaluation for ADHD[45]. At present, however, both structural and functional neuroimaging data on ADHD are inconclusive, owing in part to the use of different imaging technologies across studies and to a lack of adolescent and adult data[44]. In addition, most imaging studies of ADHD are underpowered, using samples of fewer than 20 subjects per group[44].

Treatment of ADHD

Despite the complexity of ADHD diagnosis, there are effective treatments for children that have been diagnosed with ADHD. In the United States and increasingly in Europe, psychostimulants are first-line treatments for the disorder. These drugs have been shown to be more effective at treating ADHD symptoms than behavioural therapy alone, and also more effective than behavioural therapy combined with drug treatment[18]. Stimulants have been used to treat behaviour problems in children since the 1950s. In the 1970s, researchers showed that a positive response to stimulants is not limited to children with ADHD: 'normal' children show improvements in attention and focus as well[47]. Therefore, to some degree, the medications enhance performance rather than treating the specific psychopathology.

How stimulants improve focus, attention and impulsive behaviour is still poorly understood. They are generally thought to affect brain sites associated with attention and impulse control, including the prefrontal cortex, the striatum and the cerebellar vermis[48–50]. Psychostimulant action is closely associated with the dopamine and noradrenaline systems: they bind preferentially to dopamine transporters to prevent dopamine reuptake into presynaptic nerve endings[51,52]. Both the dopamine and the noradrenaline systems are implicated in cognitive deficits that are related to ADHD, such as poor working memory and the inability to appropriately inhibit responses[33]. In the future, pharmacofMRI studies could be used to correlate neural activity during cognitive tasks to medication effects and, potentially, to tailor specific drug treatments to the particular patient[33].

Stimulants are administered in long- or short-acting forms; most children now use the long-acting forms, with effects that last 8–10 hours. Although stimulant use is associated with short-term improvements on cognitive tasks, prolonged use has not been found to be associated with long-term improvements in academic achievement when compared with baseline performance[53,54].

Stimulant drug treatment for children was long considered to be relatively safe[55]. Common side effects are usually mild, and include appetite suppression and insomnia. Recently, however, more-serious side effects have led to new US Food and Drug Administration (FDA) warnings. Since February 2007 all FDA-approved drug treatments for ADHD (methylphenidate, dexamphetamine and atomoxetine) have carried a warning that their use can involve risk for cardiovascular effects, growth suppression and the development of psychosis or other psychiatric conditions. Rare cases of sudden death have been reported among children using stimulant medications for ADHD. The FDA warns that the use of these medications by children with heart conditions should be avoided or undertaken with great caution[56].

The debate over ADHD and stimulant drugs

The global rise in ADHD diagnosis in children and the increasing rates of stimulant prescription have led to a vigorous, often polemic, debate over the validity of the ADHD diagnosis and the justification for drug treatment. This divisive debate no longer accurately reflects the state of scientific understanding of ADHD, which highlights the complexity and heterogeneity of the disorder. The remainder of this article focuses on long-standing social and ethical concerns over ADHD and highlights areas of potentially productive intersection between these concerns and the goals of scientific research.

The validity of diagnosis

Diagnoses of psychiatric disorders are controversial because they are based on clinical assessment of behavioural symptoms: there are no laboratory tests to determine unequivocally whether a subject has the disorder. In the case of ADHD, this problem is exacerbated by the fact that ADHD symptoms are difficult to distinguish from normal childhood behaviours[41]. As long as there is no clear and indisputable scientific rationale for the growing rates of ADHD diagnosis and treatment in children[4], the validity of ADHD diagnosis will continue to come under social and ethical scrutiny.

One school of thought argues that the diagnosis is frequently used to serve social or cultural purposes, such as bringing deviant or socially undesirable behaviour under medical surveillance and control[57]. Higher than average ADHD prevalence rates in the United States have been used to support claims that ADHD is a product of Western culture[58]. These arguments, which highlight the ways in which ADHD diagnosis and prevalence rates might reflect social and cultural biases, are not necessarily in opposition to the notion that ADHD is a real illness[59].

The 'science side' of the debate over ADHD diagnosis has tended to respond to diagnostic-validity challenges by asserting that ADHD is, in fact, a bona fide mental disorder[60] and by avoiding discussion of its problematics, including the potential social and cultural biases[61] (see also BOX 1). This is an ethical problem in so far as clarity about the state of the science with regards to the ADHD diagnosis is part of scientists' responsibility to the public. It is also a position that treats ADHD diagnosis as though it were a concrete representation of disorder, rather than an abstract approximation. Thus, opportunities to combine scientific and social expertise to work towards more-accurate diagnoses and diagnostic methods are overlooked.

Social scientists and scientists can work together in two areas that are currently problematic in ADHD diagnosis: standardization and consistency. A number of authoritative groups, including the American Association of Pediatrics (AAP), the UK National Institute of Clinical Excellence (NICE) and the European Network on Hyperkinetic Disorders (Eunethydis), are engaged in efforts to standardize diagnoses[62–64]. Implementing standardized diagnoses poses challenges that are best addressed through a combination of qualitative and quantitative social analyses[65]. Implementation strategies will need to be sensitive to social and indi-

Glossary

Conduct disorder
A childhood behaviour disorder characterized by persistent aggressive or anti-social behaviour that disrupts the child's environment and impairs his or her functioning.

Connors Parent/Teacher Rating Scales
Rating scales that are used to check for symptoms of ADHD. Ideally they are filled out by both teachers and parents to assist in measuring a child's behaviour and comparing it with that of other children of the same age.

Masculinity stereotypes
Sets of rigid beliefs about social roles, behaviours, activities and styles of self-presentation that are associated with being male.

Mothering ideology
A pervasive, often unconscious, set of cultural beliefs and prescriptions about what constitutes good mothering and a good mother.

Oppositional defiant disorder
A childhood behaviour disorder characterized by a persistent pattern of negative, hostile or defiant behaviour that impairs the child's social and academic functioning.

vidual variables that influence the uptake of practice innovations and the translation of evidence-based medicine into practice. These variables can be either constraining or adaptive[66] and are dependent in part on the nature, beliefs and practices of healthcare organizations, the authority with which the directive to innovate is communicated, the behaviour and beliefs of individuals in the organization, and the type of facilitation that is required to enable the change process[67,68].

Anticipation and analysis of potential barriers to diagnostic standardization will be likely to expedite implementation. However, the research that is available is based largely on Anglo-American data; little is known about relevant institutional, social and individual practices in other national contexts — particularly in the developing world, where rates of ADHD diagnoses are increasing. Exploratory qualitative studies could build relevant social theory that would guide culturally sensitive implementation strategies. The effectiveness of these strategies and their regional, national and international impact would require assessment using standardized outcome variables. Similarly, social-science–science research collaborations that focus on regional variations in ADHD diagnoses have the potential to illuminate the problem of inconsistency in ADHD diagnoses within particular populations.

Regional and global variations in ADHD diagnosis suggest that a distinction should be made between the causes of ADHD and the causes of over- and under-diagnosis of ADHD. Although there is little systematic understanding of this latter problem, it is clear that there are important social influences. Some of these are well established, including demographic factors, such as ethnicity, education level and socioeconomic status[69–71]; practitioner factors[72]; and geographic factors, including access to psychiatric services[70,73]. The influence of other social factors in ADHD diagnosis — including community factors, such as pressure within and pressure on schools[3,74], and family factors, such as parental expectations[75] — is under-researched. Cultural trends, such as mothering ideology and masculinity stereotypes, have also been proposed to influence rates of ADHD diagnosis[76–78]. Data on these influences are derived from studies using a variety of methodological approaches, and thus the relative impact of these factors is difficult to assess.

Macrosocial analyses, focusing on broad national, state or regional factors, are also being carried out to investigate the impact of national policies and programmes on ADHD diagnosis. In the United States, for example, state and federal policies arguably have a significant effect on the rates of ADHD diagnosis. The US Individuals with Disabilities Act (IDEA) provides a child who has ADHD with additional educational resources, which potentially benefits both the child and their teacher[79]. The US managed healthcare system can also be seen as an important factor in psychiatric diagnoses. Managed care encourages categorical diagnoses and quick, cheap treatments — drugs rather than behavioural therapy[80]. Finally, the US pharmaceutical industry can also influence ADHD diagnoses by marketing drugs directly to the public through direct-to-consumer (DTC) advertising[81].

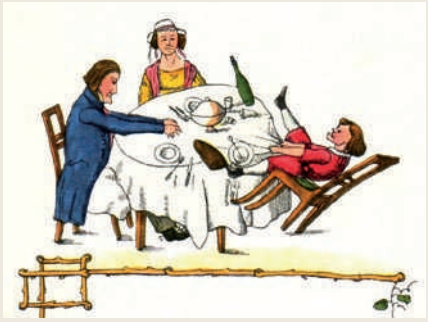
Further analysis of macro- and micro-social factors (such as school, family and community influences) in ADHD diagnosis can contribute substantially to the scientific problem of standardization and consistency in ADHD diagnosis. Resolution of these problems will have important clinical and scientific implications. From a clinical perspective, children with significant needs will be more likely to be identified and properly treated. From a research perspective, minimizing phenotypic variation across genetic studies is likely to enable more successful investigations into the genetic causes of ADHD. Indeed, some researchers argue that poor and inconsistent diagnoses of psychiatric disorders might explain much of the past failure of genetic-association studies[82].

Identifying risk factors in ADHD

As the importance of environmental factors in determining ADHD outcomes becomes clearer, scientific and social science expertise can fruitfully intersect in planned prospective studies of ADHD. In order to access the large samples that are required to detect the complex influences of environmental factors and gene–environment interactions in ADHD, future research is likely to draw on data from large national birth cohort studies, such as the planned US National Children's Study (NCS). By engaging a multidisciplinary research team and by developing innovative qualitative and quantitative research methods to conceptualize environmental risk and protective factors, test social and scientific hypotheses and track ADHD phenotypes over time, it should be possible to gain further understanding of the risk factors for ADHD. This type of approach should also allow the design of interventions that are focused on environmental risk and protective factors in a specified sub-sample.

However, there are also ethical issues in identifying individual and social risk factors for ADHD. The identification of environmental and genetic risks at the individual and societal level and the implementation of

Box 1 | **History of ADHD**



To defend the validity of attention-deficit hyperactivity disorder (ADHD), scientists occasionally draw on forms of evidence that have popular appeal but that are unfortunately palpably unscientific. For example, the National Institute of Mental Health webpage on ADHD opens with a historical narrative about the first descriptions of ADHD, attributed to Dr Heinrich Hoffman in 1845 and Sir George Still in 1902. This story of the origin of ADHD diagnosis is repeated in countless articles, books and websites and is used as evidence that the contemporary ADHD diagnosis is 'real' — in effect proposing that if the diagnosis is old it must be real. This conclusion is neither logical nor scientific. Moreover, Hoffman and Still were not actually describing ADHD as the diagnosis did not exist at the time. Both physicians describe behaviours in children that overlap with the symptom cluster that defines contemporary ADHD. Hoffman understood these behaviours to be sufficiently common (that is, not abnormal) that he depicted them in a macabre illustrated children's book that has been a bestseller for generations (see figure)[103]. His popular character, Fidgety Phil (*Zappel Philipp*), has warned generations of children about the consequences of fidgeting at the table. Still attributed the behaviours he observed to "a lack of moral control" in children, an interpretation that was aligned with contemporary eugenic theories about individuals who were 'moral defectives' by virtue of heredity[104–106]. Neither Hoffman's nor Still's descriptions provide any empirical evidence for the validity of ADHD; paradoxically, they do provide evidence that the interpretation and classification of behaviour is culturally and historically embedded. Figure reproduced, with permission, from REF. 103 © (2006) Belitha Press.

interventions are not value-free activities[83]. Individuals, families and social groups could potentially be labelled and stigmatized by such identification and might therefore resist interventions[84,85]. For example, ADHD is increasingly considered both a diagnosis and a biomarker of risk for more-severe behaviours, such as substance abuse, antisocial behaviour and criminality[86–88]. Diagnosis on the basis of risk could have long-term stigmatizing consequences, as individuals will be viewed not only in terms of their current symptoms but also in terms of their potential future dysfunctional behaviour[89]. At-risk children could become eligible for pre-symptomatic treatments, which could include drug treatments. It will be important to be cautious about bestowing 'scientific certainty' on these emerging biomarkers, especially if they become part of DSM diagnoses. Emphasizing the complexity of ADHD aetiology is likely to minimize social and ethical harms and enable positive interventions when appropriate.

Box 2 | **Neuroenhancement**

Should stimulant drug use be limited to children who meet diagnostic criteria for attention-deficit hyperactivity disorder (ADHD)? Stimulant drugs can improve attention and focus in healthy individuals as well as in children that have been diagnosed with ADHD[47]. Stimulants can also confer a short-term positive effect on academic performance[107]. The benefits of stimulants and other psychotropic drugs are helping to change ideas about normality, identity and individual improvement. In this context, the broad benefits of stimulant drugs mean that a valid diagnosis is no longer the only justification for stimulant drug use. Among US university students, stimulants are increasingly used as performance enhancers in exam and other academic situations[108,109]. UK academics admit to using stimulants and admit to desiring more performance enhancing drugs[110]. A recent informal poll in *Nature* found that most readers supported people being able to take cognitive enhancers if they wanted to[111].

Use of stimulants as cognitive enhancers in children is not equivalent to use among consenting adults, and the particular ethical implications of such practices should be scrutinized. However, cognitive enhancement in children must be acknowledged as a growing social practice that currently lacks regulation. This increases the potential for physical and ethical harms to children. One possible solution is that cognitive enhancement in children be introduced as part of clinical services, with appropriate boundaries and safeguards in place[112].

Ethical aspects of medicating children

In the future, better diagnoses and more-comprehensive understanding of ADHD aetiology are likely to have a positive impact on treatments for ADHD. At this time, however, the state of scientific understanding is not sufficient to overcome the problem of over-diagnosis of ADHD and overuse of stimulant drug treatments. In this context, it is necessary to evaluate the ethics of medicating children for ADHD.

Safety is a paramount ethical issue in psychotropic drug treatments for children with ADHD. Children are not small adults; nevertheless, most of the psychotropic drugs that are prescribed to children have only been tested on adults[90]. Although stimulants have been used to treat childhood behavioural problems since the 1930s[81], there have been few systematic longitudinal scientific studies of the long-term effects of stimulant drug use in children. Moreover, an increasing number of children are taking not just a single psychotropic drug, but a combination of these drugs[91]. The fact that there are no safety data available for drug cocktails does not dissuade parents and clinicians from using these drugs off-label in children, in increasing quantities and in ever younger populations of children[91–93]. The FDA has attempted to resolve this problem by providing 6-month patent extensions to drug companies that conduct follow-up studies in children[94]. However, the pharmaceutical industry selectively reveals psychotropic drug trial results and has concealed unfavourable safety data[95]. These are compelling reasons why careful, systematic follow-up of children taking psychotropic drugs is essential.

In addition to the potential physical harm that could be caused by stimulant drug use, potential moral harms also need to be considered. These include threats to an individual's autonomy and identity, and the imposition of stigma. A good deal of debate has revolved around these issues[96–98], but few of the arguments that have been presented are supported by detailed empirical evidence. Instead, stimulant drugs have become the lynchpin of a set of arguments centred on the problem of psychotropic drug treatments in childhood. These nurture–neuroethics arguments base notions of responsibility for care (nurture) of the child on a set of largely unexamined ideas about the nature of childhood and the nature of children. Childhood is frequently depicted as an ideal state of innocence and freedom, with children as passive subjects in need of protection. Stimulant drugs are seen as potential threats to children's right to this particular experience of childhood[99,100].

The protective intuition of nurture–neuroethics arguments is valuable and relevant in the context of drug interventions for children. However, in the case of stimulant drugs it may encourage overemphasis on the harms of diagnosis and drug intervention, and a superficial understanding of the benefits. Evidence from two small in-depth studies into the social and ethical implications of psychotropic drug treatment suggest that children with ADHD express desire for psychotropic drugs[101,102]; they successfully negotiate the stigma around drug treatment and they tend not to believe that the medication threatens their capacity to originate and direct actions for given purposes. ADHD diagnosis and stimulant drug use have been shown to affect children's concepts of identity and personal authenticity, but the available evidence suggests that these effects are largely positive for most children, at least until they reach adolescence.

There is an urgent need for a body of systematic empirical research that responds to concerns about the social and ethical risks of drug and other treatments for children with ADHD (one such study, funded by the Wellcome Trust, is ongoing — see the VOICES website for details). The largest study of ADHD treatment to date — the National Institute of Mental Health (NIMH) Multimodal Treatment Study (MTA) — includes limited investigation of the social consequences of different treatments for ADHD but no investigation of ethical consequences. Social and ethical consequences of treatment arguably influence treatment outcomes and treatment compliance. The MTA study does not include qualitative investigations of children's experiences with different treatments and with different patient management approaches over time, which could inform understanding of treatment outcomes and clinical practice. Moreover, the MTA does not include ethical analysis of children's experiences as study participants, an area that urgently requires investigation now that more children are being enrolled in neuroscience studies and in clinical trials for psychotropic drug treatments. Ethical issues — such as children's understanding of informed consent, age-related competencies to assess treatments, and treatment-related decision-making capacity — are significantly under-researched, particularly in children with cognitive and other disabilities. The omission of an ELSI (ethical, legal and social implications) component in the MTA represents a missed opportunity to combine social

and scientific expertise to increase knowledge and understanding in vitally important and under-researched areas.

Given the current and certainly the future impact of psychotropic drug use on the lives of both children and adults (BOX 2), the omission of social and ethical analyses in national research agendas seems an irresponsible oversight.

Conclusion and outlook

Drug treatments for ADHD are being rapidly translated into the fabric of daily life. This translation occurs at the science–society interface, and its social, clinical and ethical drivers and effects, as well as its social, political, educational and clinical scaffolding, require close investigation if we are to build appropriate models of ADHD that take into account both the biological and the social dimensions of the disorder.

The research goals identified here are dependent on close interactions and collaborations between social scientists, ethicists, scientists and clinicians. To keep pace with the developments in psychiatry and neuroscience, the science–society divide needs to be dismantled not just in theory but also in practice. Scientists already contribute to this effort in several ways: by considering and publicizing the social and ethical implications of their work, by clearly communicating the promises and limitations of their research, and by eschewing reductionist and determinist accounts of behaviour and personhood. It is also essential that they engage with social scientists and ethicists in research, to establish an empirical evidence base from which to assess the risks and benefits of psychotropic drugs for children.

Multidisciplinary approaches to ADHD have begun at the conceptual level and are being implemented at the level of research. For example, The Hastings Center, a US ethics institution, has received US National Institutes of Health funds to convene an interdisciplinary working group on the problem of diagnosis and psychotropic drug treatments in paediatric psychiatry. In the UK, the recent NICE ADHD Diagnosis Guideline included social scientists as special advisors and consultants. This interaction has resulted in the creation of a multidisciplinary national research group on ADHD, funded by the Mental Health Research Network. These examples underline the critical role of government and charitable funding mechanisms in enabling multidisciplinary approaches to investigate childhood psychiatric disorders and their treatments.

Such approaches will undoubtedly contribute to our understanding of psychiatric disorders and the social, ethical and physical consequences of medicating children.

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DATABASES

Entrez Gene: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene
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FURTHER INFORMATION

Ilina Singh's homepage: http://www.lse.ac.uk/collections/BIOS/whosWho/Singh.htm
NIMH Multimodal Treatment Study: http://www.nimh.nih.gov/health/trials/nimh-research-on-treatment-for-attention-deficit-hyperactivity-disorder-adhd-questions-and-answers-about-the-multimodal-treatmen.shtml
NIMH webpage on ADHD: http://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml
US National Children's Study: http://www.nationalchildrensstudy.gov/Pages/default.aspx
Voices Study (Voices On Identity, Childhood, Ethics and Stimulants): http://www.addingvoices.com/

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ERRATUM

Beyond polemics: science and ethics of ADHD

Ilina Singh

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On page 959 of the above article, figure 2 is incorrectly cited as being reproduced from reference 115. The sentence should have read:

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