ADHD in Adults

Characterization, Diagnosis, and Treatment

EDITED BY
Jan K. Buitelaar
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Philip Asherson

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Preface

Reviewing adult ADHD: Reintegration after differentiation

Originally, attention-deficit hyperactivity disorder (ADHD; formerly called minimal brain damage/dysfunction) was considered to be a childhood disorder and was therefore not diagnosed in adults. This concept that ADHD was a child-only disorder began to change in the 1970s. For the first time, two preliminary reports in 1976 on the nature of ADHD symptoms and psychosocial impairments in adults with a past history of childhood ADHD argued that ADHD might not always be outgrown in adulthood. The authors emphasized many similarities between ADHD in children and in adults in patterns of core symptoms and comorbidity, association with impairments and cognitive performance measures, and response to medication (Hechtman et al., 1976; Wood et al., 1976).

Subsequently, in 1980, the category of attention deficit disorder (ADD), residual type, was defined in *DSM-III* (American Psychiatric Association, 1980); this category provided the first opportunity to make a formal diagnosis of ADHD in adults with a past history of ADD and persisting attention and concentration problems, without a requirement of persisting hyperactivity symptoms. This diagnostic possibility must have served a purpose in practice, because its removal in the *DSM-III-R* (American Psychiatric Association, 1987) led to a request from a number of researchers and clinicians to restore it (Shaffer, 1994); efforts followed to define appropriate diagnostic criteria for ADHD in adults (Ward, Wender, & Reimherr, 1993; Wender, 1987). Although the category of ADD, residual type, was not restored in the *DSM-IV*, the *DSM-IV* ADHD criteria were modified in such a way that they could be applied more easily to adults (American Psychiatric Association, 1994).

Since then, the acceptance of adult ADHD by the professional community and the general public has been growing (Jaffe, 1995). Several longitudinal follow-up studies convincingly showed that ADHD symptoms persist in a significant proportion of adults with a history of childhood ADHD (Mannuzza et al., 1993, 1997, 1998; Weiss & Hechtman, 1993; Weiss et al., 1985). These studies were important in establishing that ADHD often persists into adulthood, with age-related changes in the way that the characteristic symptoms of the disorder present in adults.

The importance of diagnosing ADHD in adults was further supported by studies on treatment efficacy. Studies undertaken to investigate whether psychostimulant treatments were effective in adults with ADHD reported comparable effect sizes to those seen in children (Arnold, Strobl, & Weisenberg, 1972; Mattes, Boswell, & Oliver, 1984; Wender, Reimherr, & Wood, 1981; Wender, Wood, & Reimherr, 1985; Wood et al., 1976).

A landmark in the recognition of adult ADHD was the study that demonstrated significant differences in the cerebral glucose metabolism of adults with ADHD compared to control subjects (Zametkin et al., 1990). This study was innovative in two ways: it applied the new neuroimaging research paradigm to ADHD, and it did so in a sample of adults instead of children. The fMRI study of Bush et al. in 1999 – the first to demonstrate the absence of inhibitory activity of the anterior cingulate in ADHD – was carried out in adults as well.

In addition to its recognition in clinical practice, adult ADHD has developed into a research field of interest in its own right. In the last decade, the number of scientific reports on adult ADHD has increased exponentially, as shown in Figure 1.

In this exponential growth we also witness an increasing differentiation. Investigators are increasingly focusing and making progress on specific subtopics with respect to adult ADHD, and it is no longer easy to oversee the entire body of knowledge on ADHD in adulthood.

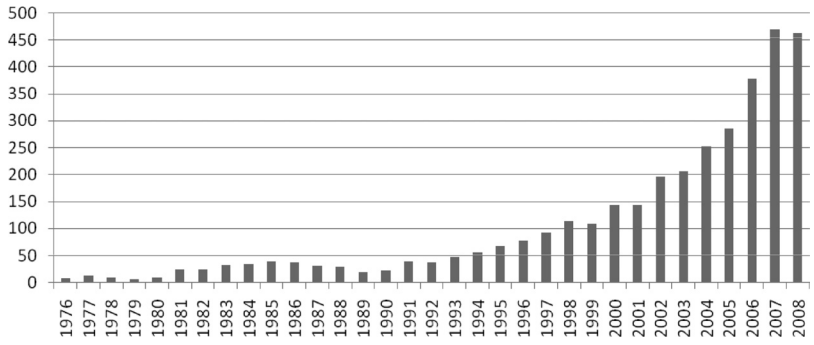

Figure 1 Number of hits in Pubmed using the keywords "ADHD" and "adult."

Therefore, the time has come to integrate many of the new insights that have been achieved during recent years. Because adult ADHD is no longer exclusively an American issue, we requested experts in different fields of adult ADHD from Europe, as well as the United States, to make a contribution to an up-to-date handbook on ADHD in adulthood. From their efforts we have assembled the present collaborative transatlantic overview.

This book is divided into the following sections:

- development of adult ADHD as an epidemiological concept
- insights into the pathophysiology of adult ADHD derived from modern research methods (genetics, neuroimaging, electrophysiology)
- proper methods to assess and diagnose adult ADHD
- the most prevalent comorbid disorders of adult ADHD
- evidence-based pharmacological treatments of adult ADHD
- the most promising psychological and social treatment strategies for adult ADHD
- alternative biological treatments for adult ADHD

The final chapter anticipates the way in which the criteria for adult ADHD might change in *DSM-V*. Probably more attention will be paid to formulating separate adult criteria, thereby acknowledging the differences between the juvenile and the adult phenotype and building on the progress made in our understanding of ADHD in adults. It appears that adult ADHD has finally grown up into a mature entity with its own adult-specific challenges.

We wish to thank all of the authors who have contributed to this book and shared their present state of knowledge, which we consider of great value, with all of the potentially interested readers. We hope that the readers will share our opinion on this book's value.

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Chapter 1

The course and persistence of ADHD throughout the life-cycle

Joseph Biederman

An important step in understanding the significance and therapeutic needs of psychiatric syndromes is documenting the course of the disorder. Those individuals who have chronic forms of disorder generally suffer greater consequences as a result, have more severe forms of disorder, and require the most aggressive intervention. Over time, the perception that attention-deficit hyperactivity disorder (ADHD) is a syndrome of childhood misbehavior that wanes throughout puberty and adolescence has been challenged by volumes of research and a continual refinement of standardized diagnostic criteria.

Attempting to understand the burden of psychiatric illness across the life span is often complicated by the fact that, with the progression of time and parallel developmental maturation, the core features of a disorder may present differently. Thus the study and treatment of childhood psychopathology often require an interpretation of symptom expression that takes into account normal development. Examining ADHD across the life span presents unique challenges because the diagnostic criteria require that the disorder be evident by 7 years of age. Natural development leads to many behavioral changes throughout childhood, adolescence, and adulthood, requiring that clinically relevant research have a nuanced interpretation of symptom expression of ADHD in older subjects.

This chapter describes the history of the disorder and the current longitudinal studies of ADHD children into adulthood, with a special focus on the changing operational definition of the disorder, the reliance on the presence of hyperactivity in diagnosis, the impact of normal developmental maturation on recognizing problem behaviors at different ages, and the clinical significance of the diagnosis in older or adult subjects.

Definition and diagnostic criteria

ADHD has long been considered a behavioral disorder of childhood even if under different names. In the 1930s, hyperkinesis, impulsivity, learning disability, and short attention span were described as minimal brain damage and later as minimal brain dysfunction because these symptoms mimicked those seen in patients with frank central nervous system (CNS) injuries. In the 1950s, this label was modified to hyperactive child syndrome, with the eventual inclusion of hyperkinetic reaction of childhood in *DSM-II* in 1968 (American Psychiatric Association, 1968). Each of these labels and sets of criterion was focused exclusively on children and placed the most importance on hyperactivity and impulsivity as hallmarks of the disorder. Although the section of *DSM-II* dedicated to hyperkinetic reaction of childhood was very brief and unstructured, it remained the prevailing standard until publication of *DSM-III* in 1980 (American Psychiatric Association, 1980).

DSM-III represented a significant change in the description of the disorder and was the first to formally recognize inattention as a significant component of the disorder. Its definition also recognized developmental variability and indicated that this variability may play a role in the presentation of the disorder in individuals of different ages. Most importantly for this discussion, *DSM-III* included a residual type of ADHD that could be diagnosed in individuals with a history of meeting full criteria for the disorder, but who presented with a reduced set of symptoms, if the remaining symptoms continued to cause significant levels of impairment. Although the revision of *DSM-III* published in 1987 (American Psychiatric Association, 1987) eliminated the residual type of ADHD, this type returned in 1994 with the publication of *DSM-IV* (American Psychiatric Association, 1994), which also offered

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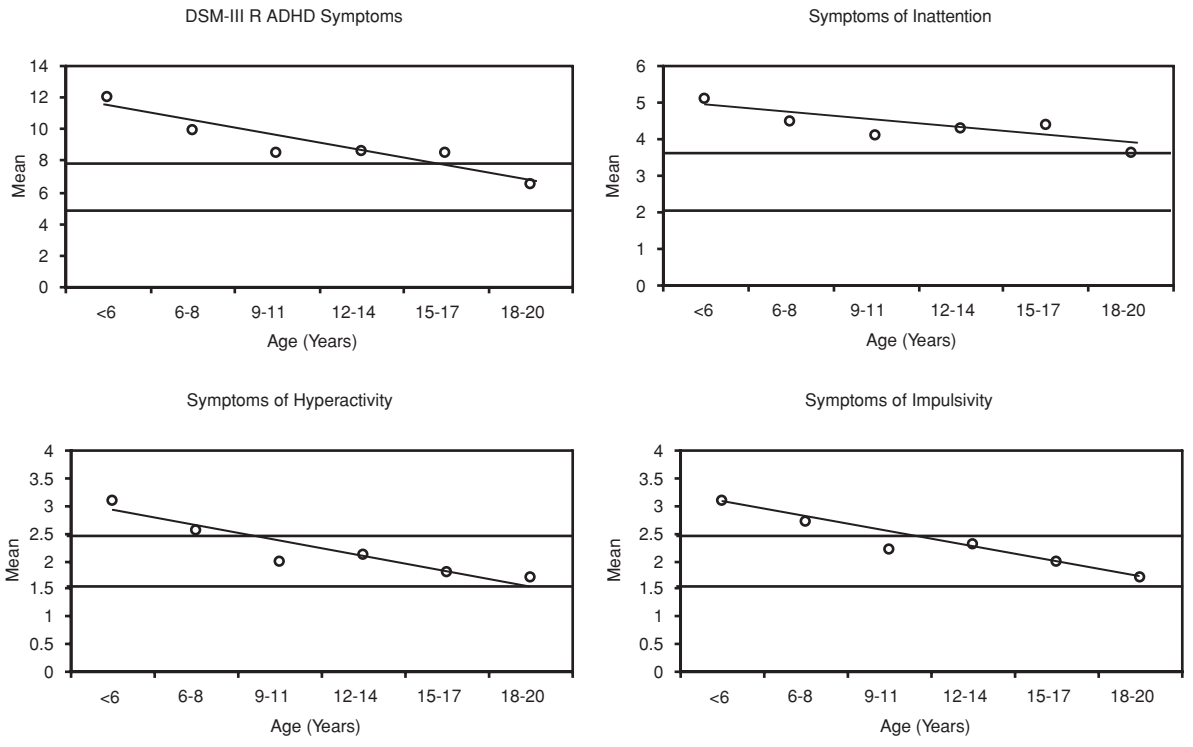

Figure 1.1 Age-dependent decline of ADHD symptoms.

criteria for specific subtypes of ADHD marked by inattention, hyperactivity/impulsivity, or both core features of the disorder.

As the field has struggled with how to characterize ADHD for the past several decades, there has been a consistent underlying notion that ADHD is not a completely remitting condition in all cases. The emphasis on hyperactivity in earlier years has also been shown to affect the rates of persistence of the disorder in prospective follow-up studies with the longest duration.

Age-dependent symptom decline

Much of the difficulty in making the diagnosis of ADHD in children arises from the fact that many of its symptoms are similar to developmentally appropriate behavior in young children. It is natural for a 4-year-old child to exhibit hyperactivity and impulsivity, for example. The diagnosis of ADHD in very young children then relies on the extent to which reported symptoms are more pronounced or prevalent than in other children of the same age. This may affect estimates of duration and definitions of chronic ADHD because as children normally outgrow much of the hyperactivity and impulsivity, the degree to which these symptoms continue to be of primary concern in making the diagnosis may also decline.

My colleagues and I specifically addressed the relative rate of decline of the core symptoms of ADHD from childhood into early adulthood to offer a developmental perspective on symptom decline (Biederman et al., 2000). ADHD subjects who returned for 4-year follow-up study were examined at multiple time points to estimate the prevalence of different symptomatic categories in different age groups. For each of the ADHD subjects (N = 128), we had five time points of symptom observations: (1) symptoms that had occurred at the disorder's onset as reported retrospectively during the baseline assessment; (2) symptoms that were currently active at baseline; (3) symptoms that were currently active at the Year One follow-up assessment; (4) symptoms that were active at the beginning of the interval covered by the 4-year follow-up based on subject recall; and (5) symptoms that were currently active at the Year Four follow-up assessment.

The mean number of ADHD symptoms in our sample of ADHD children and adolescents was

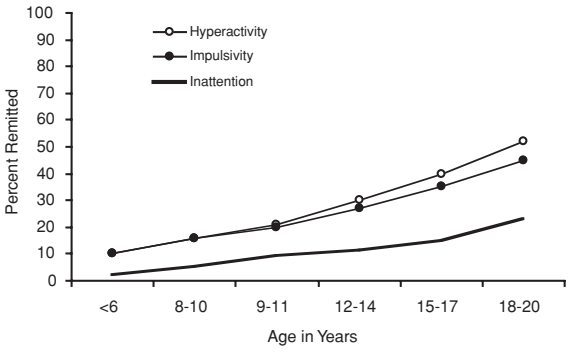

Figure 1.2 Prevalence of symptomatic remission with increasing age.

modeled as a function of age. In Figure 1.1 the predicted regression lines are plotted and horizontal lines are darkened at the value corresponding to full or subthreshold diagnoses. Age was significantly associated with symptom decline for total ADHD symptoms, as well as for each of the symptom subtypes (all Wald $\chi_{(1)}^2 > 22.9$, all p values <0.001). However, the mean number of symptoms did not fall below the subthreshold level for any of the symptom summations of any age group studied. On average, symptoms of inattention did not fall below the full threshold level by 20 years of age, whereas symptoms of hyperactivity and impulsivity did fall below the full threshold level between 9 and 11 years of age.

However, group averages do not indicate the actual prevalence of remission in each age group. Figure 1.2 presents the prevalence of symptomatic remission (having less than half of the symptoms required for the full diagnosis) for all ADHD symptoms and for each of the subtypes. We found a different rate of symptomatic decline for inattention and hyperactivity/impulsivity. Whereas symptoms of inattention declined at a very modest rate, those of hyperactivity and impulsivity remitted much more abruptly. This work demonstrated that, even in a sample of ADHD children with a high rate of symptom persistence (Biederman et al., 1996), overt symptoms of hyperactivity and impulsivity tend to decline with increasing age. Hart et al. (1995) documented a similar pattern of ADHD-subtype specific persistence: the mean number of hyperactive/impulsive symptoms declined with age, whereas the mean number of inattentive symptoms remained stable from age 8 to 15 years. Thus, it seems that the persistence of ADHD is contingent on continued inattention more than on overt hyperactivity or impulsivity.

Impact of symptom decline patterns on rates of persistence

A relatively large number of studies have been published that estimate the persistence of ADHD throughout adolescence and adulthood. Table 1.1 presents the pertinent results from each these studies. Clearly, the rate of ADHD at follow-up varies considerably from one study to the next. For example, Mannuzza et al. (1998) reported that at follow-up 4% of previously hyperactive boys continued to have ADHD, whereas Hart et al. (1995) found that 85% of ADHD cases met criteria for ADHD at follow-up. However, these divergent findings should not be surprising considering the significant heterogeneity between these studies in diagnostic criteria employed, duration of follow-up, and age of the sample at follow-up.

Table 1.1 also indicates that the changing diagnostic classification of ADHD over the years has influenced estimates of persistence of the disorder. The studies listed in Table 1.1 are categorized by the diagnostic system that was used to ascertain the samples. Samples in studies initiated under *DSM-II* had the lowest rate of persistence, whereas the rate of persistence in samples identified under *DSM-III-R* was the highest. This finding is consistent with our earlier work showing the increased rate of remission from hyperactive and impulsive symptoms relative to symptoms of inattention.

Perhaps one of the most important variables is age at follow-up – certainly a 5-year follow-up of 12-year-olds will result in a higher prevalence of ADHD than a 5-year follow-up of 25-year-olds. Hill and Schoener (1996) used this level of heterogeneity in age to estimate the expected rate of ADHD in older populations. They conducted a secondary data analysis of a subset of the studies presented in Table 1.1, selecting those in which the original diagnoses were made concurrently with the creation of the studies' baseline in childhood and in which the follow-up reported the persistence of standardized assessments of ADHD. Hill and Schoener fit a model to these data that predicted an exponential decline in the rate of ADHD and estimated the rate of adult ADHD to range from about 0.8% at age 20 to 0.05% at age 40. At first glance, these results seem to provide strong support for the idea that ADHD is essentially a remitting disorder.

Alternatively, the explanation for these discrepant findings may be that the use of different methods to determine diagnostic status at follow-up led to

Table 1.1 Published studies estimating the persistence of ADHD throughout adolescence and adulthood

	Age range or mean at baseline (years)	Age at follow-up (years)	ADHD persistence		Follow-up ADHD diagnosis
***DSM-II* diagnosis at baseline**					
Mendelson et al. (1971)	9.9	13.4	42	50	*DSM-II*
Borland & Heckman (1976)	7.5	30.4	10	50*	*DSM-II*
Mannuzza & Gittelman (1984)	7.9	17.4	12	33	*DSM-III*
Mannuzza (1984)	7.9	17.4	13	36*	*DSM-III*
Gittelman & Mannuzza (1985)	9.3	18.3	31	31	*DSM-III*
Gittelman (1985)	9.3	18.3	40	40*	*DSM-III*
Mannuzza et al. (1991)	7.3	18.5	21	22	*DSM-III*
Mannuzza et al. (1991)	7.3	18.5	41	43*	*DSM-III*
Mannuzza et al. (1993)	9.3	25.5	7	8	*DSM-III, III-R*
Mannuzza et al. (1993)	9.3	25.5	10	11*	*DSM-III, III-R*
Mannuzza et al. (1998)	7.3	24.1	3	4	*DSM- III-R*
Mannuzza et al. (1998)	7.3	24.1	3	4*	*DSM- III-R*
Lambert et al. (1987)	7.7	14.3	25	43	*DSM-III*
Lambert (1988)	9.3	18.3	47	80*	*DSM-III*
Feldman et al. (1979).	10.0	15.5	35	43	*DSM-II*
August et al. (1983)	10.7	14.2	19	86*	*DSM-III*
Weiss et al. (1985)	6–12	25.1	42	66*	*DSM-III*
Yan (1996)	10.0	25.5	140	70*	*DSM- III-R*
Combined estimate			39 ± 21%		
***DSM-III* diagnosis at baseline**					
Cantwell & Baker (1989)	5.5	9.7	28	80	*DSM-III*
Offord et al. (1992)	4–12	8–16	16	34	*DSM-III*
Claude & Firestone (1995)	7.3	19.7	26	50	*DSM- III-R*
Rasmussen & Gillberg (2000)	7	22	28	56*	*DSM-IV*
Rasmussen & Gillberg (2000)	7	22	24	48	*DSM-IV*
Combined estimate			53 ± 41%		
***DSM-III-R* diagnosis at baseline**					
Barkley et al. (1990)	4–12	14.9	88	72	*DSM- III-R*
Barkley et al. (1990)	4–12	14.9	102	83*	*DSM- III-R*
Barkley et al. (2002)	4–12	21.1	78	58	*DSM-IV*
Barkley et al. (2002)	4–12	21.1	89	66*	*DSM-IV*
Har et al. (1995)	9.4	10.4	89	84	*DSM-III-R*
Hart et al. (1995)	9.4	11.4	90	85	*DSM-III-R*
Hart et al. (1995)	9.4	12.4	92	77	*DSM-III-R*
Biederman et al. (1996)	10.5	14.5	109	85*	*DSM-III-R*
Biederman et al. (1996)	10.5	14.5	78	61	*DSM-III-R*
Biederman (2006)	10.5	22.8	63	58*	*DSM-IV*
Biederman (2006)	11.2	16.4	101	82*	*DSM-IV*
Combined estimate			73 ± 27%%		

*Residual ADHD diagnosis.

different results. Because the number of symptoms present determines diagnostic status, different ways of interpreting symptom decline could lead to drastically different results. Focusing only on those subjects who continue to meet full diagnostic criteria may inflate the rate of remission by requiring a threshold that is too high because one still expects older subjects to present with significant rates of hyperactivity or impulsivity.

In our previous analysis of symptom decline (Biederman et al., 2000), we also assessed three levels of remission: syndromatic, symptomatic, and functional. *Syndromatic* remission refers to the loss of full diagnostic status, *symptomatic* remission refers to the loss of partial diagnostic status, and functional remission refers to the loss of partial diagnostic status plus functional recovery (full recovery). In our data, the rate of remission from the full disorder (syndromatic remission) was quite high, with 60% of our subjects aged 18 to 20 years old no longer meeting criteria for ADHD (Biederman et al., 2000). However, nearly one-third of subjects were still experiencing some ADHD symptoms (a symptomatic remission rate of 30%), and the majority of ADHD subjects continued to report low levels of functioning despite remission of the full diagnostic criteria (a functional remission rate of only 10%).

Therefore, Hill and Schoener (1996) may have been far too optimistic in declaring that the prevalence of ADHD in adult samples was nearly nonexistent. An expanded analysis of the literature supports the notion that in many studies subjects fail to reach symptomatic remission. Faraone et al. (2006) revisited Hill and Schoener's analyses by including studies that reported the follow-up rate of ADHD-residual type (analogous to symptomatic persistence). It should not be surprising that the inclusion of the less stringent definition of persistence resulted in higher rates in older subjects (see Fig. 1.3). Their meta-analysis found that, of children diagnosed with ADHD during childhood, 62% will continue to be symptomatic although only 19% would continue to meet full diagnostic criteria at age 25.

Although high rates of syndromatic remission indicate that individuals with ADHD frequently lose full diagnostic status, these figures may be misleading because they cannot distinguish individuals who fall just below the diagnostic threshold from those with very few active symptoms of the disorder. It is technically correct that those diagnosed with

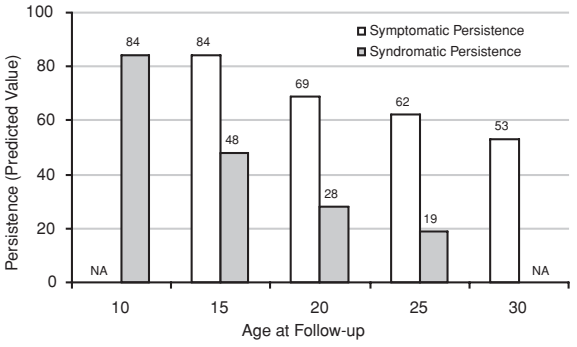

Figure 1.3 Predicted rate of persistence in follow-up studies of ADHD children.

ADHD in childhood who reach adulthood with one less symptom of the disorder may no longer satisfy criteria for ADHD, but it is clinically dubious to equate the absence of full syndromatic status with full recovery.

Thus, as expected from the work of Fischer (1997) and Biederman et al. (2000), the apparent prognosis of ADHD depends on what definition of persistence one uses. Our work examining differential rates of decline of ADHD symptom cores indicates that the choice of definition should be influenced by an individual's age and developmental expectations regarding hyperactivity, impulsivity, and inattention.

Clinical significance of ADHD in adults

If adult ADHD is a clinically significant disorder, then adults with ADHD should show functional impairments in multiple domains. Several studies suggest this to be the case. In an early study, Borland and Heckman (1976) compared ADHD adults with their non-ADHD siblings. The ADHD adults had lower socioeconomic status, more work difficulties, and more frequent job changes. Morrison (1980a, 1980b) compared ADHD adults with psychiatric controls matched for age and sex. The ADHD adults had fewer years of education and lower rates of professional employment. Similarly, others have shown that, among patients with substance use disorders, ADHD predicts social maladjustment, immaturity, fewer social assets, lower occupational achievement, and high rates of separation and divorce (Alterman et al., 1982; Eyre et al., 1982; De Obaldia & Parsons, 1984; Tarter, 1982; Wilens et al., 1998).

Murphy and Barkley (1996) compared 172 ADHD adults with 30 non-ADHD adults. The ADHD adults

reported more psychological maladjustment, more speeding violations, and more frequent changes in employment. Compared with the non-ADHD adults, more ADHD adults had had their drivers license suspended, had performed poorly at work, and had quit or been fired from their job. Moreover, the ADHD adults were more likely to have had multiple marriages.

Barkley et al. (1996) evaluated the motor vehicle driving knowledge and skills and negative driving outcomes of older teens and young adults with ADHD. Although the young adults with ADHD showed no deficits in driving knowledge, they had elevated rates of speeding citations, suspended licenses, crashes, and accidents causing bodily injury compared to those without ADHD. They were more likely to be rated by themselves and others as having poorer driving habits. In addition, on a computer-simulated driving test, young adults with ADHD had more crashes, scrapes, and erratic steering.

Given that academic underachievement is a well-known correlate of ADHD in childhood (Hinshaw, 1992), ADHD adults ought to have histories reflecting school problems. Several studies have shown this to be so. Our work demonstrated that, compared with control adults, ADHD adults had significantly higher rates of repeated grades, tutoring, placement in special classes, and reading disability. Similarly, Murphy and Barkley (1996) showed that adults with ADHD had histories marked by poorer educational performance and more frequent school disciplinary actions against them. Notably, in addition to showing an increased likelihood of having a history of school failure, Seidman et al. (1998) demonstrated that this history could not be accounted for by age, learning disabilities, psychiatric comorbidity, or gender.

We recently conducted a survey of 1000 ADHD and non-ADHD adults in the United States (Biederman et al., 2006). This survey, which had the largest sample of community-diagnosed adults with ADHD ever studied, showed that adults with self-reported ADHD in the community suffer from significant impairments across multiple domains of functioning. We found adult ADHD to be associated with histories of school failure, occupational impairment, substance use, traffic violations, arrests, decreased quality of life, and sexual problems. Taken together, these findings support the idea that, even in those adults diagnosed in the community, ADHD is a clinically significant and highly disabling disorder (Biederman et al., 2006).

Impact of treatment on course

Although there is a wealth of research on the efficacy of pharmacotherapy in treating symptoms of ADHD (Spencer et al., 1996, 2002), we do not know if treatment during childhood has an impact on the symptomatic or functional remission from the disorder as described here. In fact we are unable to assess the impact of treatment in the short or long term in naturalistic studies because exposure to therapy is not randomly assigned (Faraone et al., 1992). Observational research of treatment efficacy is often misleading because of confounding by indication: a situation in which severely ill patients are more likely to receive treatment so that aggressive therapy appears to be inversely associated with improvement solely due to the inability to control the allocation of treatment.

For example, subjects likely to be among remitters may be likely to receive therapy for a shorter duration because their symptoms have remitted, whereas those with persistent symptoms are more likely to have been exposed to a longer period of treatment. Under this reasonable assumption, naturalistic studies would clearly show that treatment is inversely associated with rates of remission. Research is needed that examines both the motivation for continued treatment in naturalistic follow-up studies and the impact of therapy in subjects treated in a randomized clinical trial over the long term.

Summary

At any age, ADHD may be considered a chronic disorder because its symptoms may persist for a long period of time and over a wide range of settings. The use of more developmentally appropriate measures of ADHD in adolescents and adults reveals that a sizable proportion of children with the disorder will continue to exhibit impairing symptoms of the disorder into adulthood. The impact of ADHD on society is enormous in terms of financial cost, stress to families, impact on academic and vocational activities, as well as negative effects on self-esteem. Because the disorder is not episodic but frequently chronic, ADHD may be a relatively common psychiatric disorder of adulthood in reference to other disorders.

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Chapter 2

The prevalence and correlates of adult ADHD

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It has long been known that attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders among children (Bird et al., 1988; Shekim et al., 1985). However, there is much less agreement about the extent to which ADHD persists into adulthood. Indeed, some authors state that adult ADHD is very rare (Shaffer, 1994), whereas others report that it is quite common (Barkley, 1997). The claim that adult ADHD is rare can be traced to theoretical discussions about the role of maturation in resolving childhood impulsivity (Cantwell, 1985). The empirical study that is consistently cited to support this claim is the influential meta-analysis carried out by Hill and Schoener (1996) of nine prospective studies of children who were diagnosed with ADHD and then followed between 4 and 16 years. The aim of the meta-analysis was to develop a mathematical model of the extent to which ADHD prevalence decreases with age. The nonlinear model developed by Hill and Schoener to fit the data in these nine studies estimated that ADHD prevalence decreases by approximately 50% every 5 years. Based on the assumption that ADHD prevalence is 4% in childhood, this model predicted that prevalence at age 40 would only be a fraction of 1%.

Subsequent critiques have argued that several methodological factors (e.g. small number of studies, nonrepresentative studies, inappropriate statistical model, sample attrition, reporting bias) introduced imprecision and potential bias into the Hill and Schoener estimates of ADHD persistence (Mannuzza, Klein, & Moulton, 2003; Sawilowsky & Musial, 1988). Leaving aside issues of change in diagnostic criteria and sample selection bias, which are endemic to adult follow-up studies of children diagnosed with ADHD in the past, the key issue in these critiques is whether to require adults to meet full diagnostic criteria or to have only some symptoms to be counted as cases. In their meta-analysis Hill and Schoener required adults to meet full diagnostic criteria, resulting in adults who had ADHD as children being classified as "remitted" even if they continued to have seriously impairing symptoms. An indication of how critical this distinction is can be seen in a subsequent short-term follow-up study of an ADHD patient sample, which found that, although only 38% of cases continued to meet full criteria for ADHD at age 19, 90% continued to have clinically significant impairment associated with remaining symptoms (Biederman, Mick, & Faraone, 2000).

Uncertainty about diagnostic criteria

It is important to note in this regard that diagnostic criteria for ADHD have never been developed specifically for adults, making it unclear what it means to meet "full criteria" for adult ADHD. In *DSM-III*, the category of residual attention-deficit disorder was defined to include adults who met full criteria for the disorder as children and have a partial syndrome as adults, but this category was removed from *DSM-III-R*. Meanwhile, a number of clinical research groups have proposed that the distribution of the three cardinal symptom clusters found among children – inattention, hyperactivity, and impulsivity – shifts in adulthood so that inattention becomes the most prominent symptom cluster, and other symptoms, such as affective lability, explosive temper, inability to tolerate stress, and dysphoria, emerge as more prominent than in childhood (Riccio et al., 2005; Wender et al., 1985). Based on this change in symptom presentation, experts agree that more research is needed to develop valid diagnostic criteria for adult ADHD (Adler & Cohen, 2004; McGough & Barkley, 2004; Wender, Wolf, & Wasserstein, 2001).

ADHD in Adults: Characterization, Diagnosis and Treatment, ed. Jan Buitelaar, Cornelis Kan and Philip Asherson. Published by Cambridge University Press.

In light of this uncertainty about diagnostic criteria, a legitimate question can be raised whether adult ADHD is a genuine disorder. The data are quite compelling that it is. This conclusion is based both on (1) clinical evidence that diagnosis, albeit fettered with the conceptual problems described in the last paragraph, is of considerable value in predicting symptom persistence and progression, severity, and treatment response, and on (2) evidence of genetic transmission and abnormalities in brain structure and function (Resnick, 2005; Seidman, Valera, & Makris, 2005; Wilens, Faraone, & Biederman, 2004).

Indirect assessments of prevalence

Given that ADHD is a genuine adult disorder, how common is ADHD in adulthood? The answer is clouded by the uncertainty associated with diagnostic issues. Because of this uncertainty, none of the many adult community psychiatric epidemiological surveys carried out over the past two decades with either the Diagnostic Interview Schedule (Robins et al., 1981) or the Composite International Diagnostic Interview (CIDI; Robins et al., 1988) included an assessment of adult ADHD. As a result, little is known about the general population epidemiology of adult manifestations of this disorder. Attempts to estimate prevalence by extrapolation from childhood prevalence estimates in conjunction with adult persistence estimates (Barkley et al., 2002; Biederman et al., 2000; Mannuzza et al., 1988; Weiss et al., 1985) or by direct estimation from small sample of adults (Murphy & Barkley, 1996) or of college students (Heiligenstein et al., 1998) have yielded prevalence estimates ranging from 1–6%. However, these estimates are all based on convenience samples.

One way to obtain a more accurate prevalence estimate would be to build on a more firm set of estimates from previous studies that linked information about prevalence in childhood with information about persistence into adulthood. Faraone and his colleagues recently reported the results of a comprehensive meta-analysis of all published follow-up studies of ADHD; it provides the best currently available estimate of persistence into adulthood (Faraone, Biederman, & Mick, 2006). This study, which was carried out along the same lines as the Hill and Schoener meta-analysis (1996), deviated from the earlier approach in distinguishing between syndromal and subsyndromal persistence of adult ADHD. The analysis showed that, whereas only a relatively small proportion of cases (approximately 15%) in the studies examined continued to meet full criteria for ADHD in adulthood, a majority (approximately two-thirds) continued to have enough symptoms and impairment to qualify for a *DSM-IV* diagnosis of ADHD in partial remission.

The population prevalence of broadly defined ADHD at age 25, then, might be expected to be roughly two-thirds as high as the prevalence in childhood, although caution is needed in making this extrapolation based on the fact that the follow-up studies examined by Faraone et al. (2006) included clinical samples in which the most serious childhood cases are presumably overrepresented. This factor is important because severity of childhood symptoms strongly predicts adult ADHD persistence (Kessler, Adler, Barkley, et al., 2005). A further complication in using this indirect way to estimate the prevalence of adult ADHD is that prevalence estimates of childhood ADHD have an extremely wide range – from as low at 1.5% to as high as 19.8% (Cuffe et al., 2001; Cuffe, Moore, & McKeown, 2005; Faraone et al., 2003; Pastor & Reuben, 2005). If we take the median of the range, which is 7–9%, we would predict that the prevalence of adult ADHD would be roughly 5–6%, but this could be an overestimate for the reason described in the first part of this paragraph.

Screening assessments of prevalence

Two recent reports described the results of general population surveys that attempted to screen for adult ADHD (Faraone & Biederman, 2005; Kooij et al., 2005). Faraone and Biederman (2005) carried out a telephone survey with 966 adults in the United States that used semi-structured research clinical interviews to assess adult ADHD using *DSM-IV* criteria. The authors estimated that 2.9% of respondents met full *DSM-IV* criteria for ADHD and that 16.4% met subthreshold criteria. Kooij et al. (2005) carried out a self-report survey of a representative sample of 1813 adults selected from an automated general practitioner registry in the Netherlands. They used a fully structured questionnaire to estimate the prevalence of adult ADHD. No clinical follow-up interviews were carried out to validate these self-reports. The authors estimated the prevalence of adult ADHD to be 1.0% when full *DSM-IV* criteria were required and 2.5% when the diagnosis was relaxed to require four rather than six current symptoms.

A direct assessment of prevalence

The NCS-R

The only published adult ADHD prevalence study that was based on a nationally representative general population sample with clinical calibration was carried out in conjunction with the US National Comorbidity Survey Replication (NCS-R; Kessler & Merikangas, 2004). A fully structured retrospective assessment of childhood ADHD and a fully structured screen for adult ADHD were both developed for use in the NCS-R as part of the revised WMH-CIDI (World Mental Health-CIDI; Kessler & Ustun, 2004). These assessments were administered face-to-face to a nationally representative sample of 3,199 people in the age range of 18–44 as part of the larger NCS-R interview. In addition, blinded clinical reappraisal follow-up interviews to diagnose adult ADHD were carried out with a probability subsample of 154 NCS-R respondents, thereby oversampling those who met criteria for adult ADHD in the fully structured assessment (Kessler, Adler, Ames, et al., 2005). Other *DSM-IV* diagnoses made in this sample with the CIDI included anxiety disorders (panic disorder, generalized anxiety disorder, agoraphobia without panic disorder, specific phobia, social phobia, post traumatic stress disorder, obsessive-compulsive disorder), mood disorders (major depressive disorder, dysthymia, bipolar disorder I or II), impulse-control disorders (oppositional-defiant disorder, conduct disorder, intermittent explosive disorder), and substance use disorders (alcohol and drug abuse and dependence).

Multiple imputation

An innovative method was used in the NCS-R to estimate the prevalence of clinician-assessed *DSM-IV* adult ADHD in the total US population aged 18–44; it took into consideration the prevalence estimate in the small clinical reappraisal, the strength of the association between the fully structured assessment and the clinical assessment in the clinical reappraisal subsample, and the distribution of responses to the structured questions in the full sample. This method, known as multiple imputation (MI; Rubin, 1987), first assigned predicted probabilities of meeting *DSM-IV* criteria for a diagnosis of adult ADHD to each respondent in the sample who did not participate in the clinical reappraisal study, based on the results of logistic regression analysis carried out in the clinical reappraisal subsample that linked responses to the fully structured questions with clinical diagnoses. After these predicted probabilities were assigned, the probability was transformed to a dichotomous case classification separately for each respondent by random selection from the binomial distribution for the predicted probability.

Estimated prevalence

A strong predictive association was found in the clinical reappraisal subsample between responses to the structured questions and the clinical diagnoses of adult ADHD (with a 0.86 area under the receiver operator characteristic curve [AUC]), thereby justifying the use of the imputation method described earlier. However, this method clearly leads to errors in classification because the AUC is less than 1.0. Although the imputation nonetheless yields an unbiased estimate of prevalence and generally conservative estimates of associations, this imprecision increases the standard error of the prevalence estimate. The MI method deals with this problem by using simulation to estimate standard errors of parameter estimates. This is done by repeating the entire imputation process a number of times (10 times in the NCS-R application), beginning with the selection of a new pseudo-sample of size 154 for each replicate from the clinical reappraisal subsample and reestimation of parameter values for the prediction equation. All substantive analyses of the data were then replicated 10 times, once for each set of imputations, and the standard errors of descriptive statistics were calculated empirically by combining information about the average within-replicate variance in the parameter estimates with information about between-replicate variance in the parameter estimates.

The vast majority of NCS-R respondents in the age range 18–44 (Table 2.1, Column I) reported that they had no clinically significant problems with inattention, hyperactivity, or impulsivity during their childhood (85.8%). Smaller percentages reported either subthreshold childhood symptoms of ADHD (7.5%), full childhood criteria but no current symptoms (4.0%), or full childhood criteria in addition to current symptoms (2.6%). A strong monotonic relationship was found between this four-category WMH-CIDI classification scheme and blind clinical diagnoses of adult ADHD in the clinical calibration sample (Table 2.1, Column II). The MI-estimated prevalence of adult ADHD based on the 10 imputed case classifications of adult ADHD (standard error in parentheses) is 4.4%

Table 2.1 Distribution of adult ADHD imputation classes in the NCS-R[1] and conditional prevalence of clinician-rated adult ADHD in the clinical reappraisal subsample

ADHD risk	Total sample distribution		Conditional prevalence of adult ADHD in the clinical reappraisal subsample	
	%	(se)	%	(se)
None	85.8	(0.8)	0.0	–
Low	7.5	(0.5)	7.3	(6.4)
Medium	4.0	(0.4)	36.6	(8.9)
High	2.6	(0.4)	84.8	(7.7)
Total	100.0		4.4	(0.6)
(n)	(3199)	(154)		

[1] Part II respondents aged 18–44.

(0.6). It is noteworthy that exactly the same estimated prevalence and standard error are obtained by using a more conventional two-stage sampling adjustment.

Socio-demographic correlates

As the NCS-R sample is quite large, it was possible to go beyond simple estimation of prevalence to consider correlates of adult ADHD. ADHD was estimated to be significantly more prevalent among men than women, people with low compared to high education and family income, unmarried compared to married people, and unemployed compared to employed people (Kessler, Adler, Barkley, et al., 2006). The odds ratios (ORs) associated with these predictors were all found to be moderate in size (1.7–2.4).The strongest socio-demographic correlate of adult ADHD in the NCS-R was race-ethnicity, with non-Hispanic Blacks having significantly lower odds of the disorder than non-Hispanic Whites (0.3). No significant associations were found with age (in the 18–44 age range), region of the country, or urbanicity. The absence of an association with age is especially striking in light of the suggestion based on the Hill and Schoener (1996) meta-analysis that the prevalence of ADHD decreases by 50% every 5 years. The nationally representative NCS-R results show clearly that no such decline exists in the general population.

Comorbidity with other DSM-IV disorders

Statistically significant comorbidities were found in the NCS-R between adult ADHD and a wide range of other *DSM-IV*/CIDI anxiety, mood, impulse-control, and substance use disorders (Kessler, Adler, Barkley, et al., 2006). ORs were generally somewhat larger for comorbidities with 12-month than with lifetime disorders, suggesting indirectly that adult ADHD is associated with these disorders being somewhat more persistent than otherwise. ORs with 12-month disorders were in the range of 3.3–6.1 for mood disorders, 2.6–5.3 for anxiety disorders, 2.1–14.9 for substance disorders, and 3.8–9.8 for impulse-control disorders. Very strong ORs with 12-month drug dependence (14.9) and oppositional-defiant disorder (9.8) were especially noteworthy.

Table 2.2 Impairments in 30-day functioning associated with adult ADHD in the NCS-R[1]

	%[2]	(se)[2]	OR[3]	(95% CI)[3]
I. Basic functioning				
Self-care	7.6	(2.7)	2.2*	(1.0–4.8)
Mobility	26.7	(4.7)	3.9*	(2.3–6.8)
Cognition	29.9	(5.3)	2.6*	(1.5–4.5)
II. Instrumental functioning				
Time out of role	38.3	(4.9)	2.7*	(1.8–4.1)
Productive role functioning	35.0	(4.6)	2.1*	(1.4–3.2)
Social role functioning	18.6	(3.5)	3.5*	(2.1–5.9)

* Significant at the 0.05 level, two-sided design-based MI tests.
[1] Part II respondents aged 18–44.
[2] Percent (standard error) of adults with ADHD who have the impairment.
[3] Based on bivariate logistic regression analysis using MI to estimate odds ratios (ORs) and 95% confidence intervals (95% CI).

Associations with basic and instrumental functioning

Adult ADHD was found in the NCS-R to be significantly associated with serious difficulties in all three areas of basic functioning assessed in the WHO Disability Assessment Schedule (WHO-DAS; Chwastiak & Von Korff, 2003): self-care, mobility, and cognition (Table 2.2). ORs of these impairments for people with adult ADHD versus without adult ADHD were in the range of 2.2. Adult ADHD was also found in the NCS-R to be significantly related to all three WHO-DAS measures of disability in instrumental functioning: elevated odds of high days out of role (2.7), high impairment in productive role functioning (2.1), and high impairment in social role functioning (3.5).

Table 2.3 Twelve-month treatment among respondents with adult ADHD in the NCS-R[1]

	%	(se)
Specialty	25.9	4.4
General medical	18.8	3.4
Human services	7.4	1.5
CAM[2]	18.4	5.1
Any treatment	42.4	4.4

[1] Part II respondents aged 18–44
[2] Complementary and alternative medicine.

Associations with work performance

The NCS-R analysis also examined associations of adult ADHD with work performance (Kessler, Adler, Barkley, et al., 2005). The prevalence of ADHD among employed people (4.2) was found to be roughly comparable to prevalence in the total population, although it was higher among male than female workers and among blue-collar than white-collar workers. An analysis of work performance based on the WHO Health and Work Performance Questionnaire (Kessler, Ames, et al., 2004; Kessler, Barber, et al., 2003) showed that ADHD was associated with an enormous amount of work role impairment. At the individual level, workers with ADHD were estimated to have an annual average of 35 more lost work performance days than comparable (in terms of socio-demographics and job requirements) workers without ADHD. This negative impact of ADHD on work performance was especially pronounced among blue-collar workers, who had an annual average excess of 56 lost work performance days). At the population level, these adverse workplace effects of ADHD were projected to total 120 million lost work days and $19.5 billion lost human capital annually in the United States.

Treatment

Of respondents with adult ADHD in the NCS-R, 42.4% reported that they received treatment for problems with their mental health or substance problems at some time in the 12 months before the NCS-R interview (Table 2.3). The majority of these respondents (25.9% of all respondents with the disorder) were seen in the mental health specialty sector. A significantly higher proportion of females than males with adult ADHD received treatment for mental or substance problems in the 12 months before the interview (53.1% vs. 36.5%, $z = 2.6$, $p = 0.014$). However, comparison of reports about disorder-specific and overall treatment showed that only 25.2% of treated cases were receiving treatment for their symptoms of ADHD (22.8% of females vs. 27.7% of males, $z = 0.5$, $p = 0.598$). Because of this low proportion, only 10.9% of respondents with adult ADHD received treatment for ADHD in the 12 months before the interview (12.1% of females vs. 10.1% of males, $z = 0.4$, $p = 0.657$).

Is adult ADHD more prevalent in the United States than elsewhere in the world?

The vast majority of clinical and community epidemiological research on ADHD has been carried out in the United States, leading to an impression that ADHD is more common in the United States than in other countries (Taylor & Sandberg, 1984). However, comparative studies of the factor structure of self-reported ADHD symptoms among children in several English-speaking countries (United States, Canada, United Kingdom, Australia, and New Zealand) have found both comparable factor structures and comparable symptom prevalence estimates (Taylor, 1986; Taylor & Sandberg, 1984). A recent comprehensive review of the estimated prevalence of childhood ADHD in 50 published studies from around the world (20 in the United States and 30 in all other countries combined) concluded that the prevalence of ADHD is at least as high in some other countries as in the United States (Faraone et al., 2003).

But what of the worldwide prevalence of adult ADHD? The evidence is too scant to make an informed statement. Indeed, the only published community prevalence study of adult ADHD outside the United States is the Kooij et al. (2005) study from the Netherlands that we cited earlier. However, additional information will soon be available from the WHO WMH Survey Initiative (Demyttenaere et al., 2004), which is a series of nationally representative general population epidemiological surveys of mental disorders that were carried out in nearly 30 countries around the world (see www.hcp.med.harvard.edu/wmh). The same assessment of adult ADHD as in the NCS-R was included in a number of the WMH surveys. Although most of these surveys are still in progress, plans exist to replicate the NCS-R analyses once data become available from all of them.

Future directions

As demonstrated in this review, the epidemiological literature on adult ADHD is very limited. Only one nationally representative general population survey (the NCS-R) ever included a rigorous clinical assessment of adult ADHD. Even in that one study, the assessment did not consider ADHD in partial remission despite other evidence that that type might be considerably more common than syndromal adult ADHD (Faraone & Biederman, 2005; Faraone et al., 2006). The anticipated publication of results from the WHO World Mental Health surveys will go a long way in addressing the first of these problems, but will still not provide data on subsyndromal cases.

A more serious limitation of the existing literature is that uncertainties exist about the appropriate criteria for adult ADHD. The criteria for ADHD were developed with children in mind and offer only limited guidance regarding diagnosis of adults. This lack of guidance is of considerable concern because clinical studies make it clear that symptoms of ADHD are more heterogeneous and subtle in adults than in children (DeQuiros & Kinsbourne, 2001; Wender et al., 2001). As a result, many experts believe that the valid assessment of adult ADHD might require either an increase in the variety of symptoms assessed (Barkley, 1995), a reduction in the severity threshold for considering a symptom clinically significant (Ratey et al., 1992), or a reduction in the *DSM-IV* six-of-nine symptom requirement (McBurnett, 1997). This matter of appropriate diagnostic criteria needs to be settled before much progress can be made in epidemiological research.

Another important unresolved issue in the assessment of adult ADHD concerns the mode of assessment. Childhood ADHD is diagnosed largely on the basis of parent and teacher reports rather than self-reports because parents and teachers are both in good positions to observe child behavior and because children with ADHD often have little insight into the severity of their symptoms (Jensen et al., 1999). The situation is different for adults, for whom there is great variability in the extent to which other people observe their behavior and where access to reliable informants varies with the respondent's marital status, occupational status, and social networks; as a practical matter it is therefore necessary to base assessment largely on self-reports (Wender et al., 2001). As a result, epidemiological studies of adult ADHD have relied almost entirely on self-reports. This reliance might be problematic in that some methodological studies comparing adult self-reports versus informant reports of ADHD symptoms have documented a similar pattern of disagreement as in studies of child self-reports versus informant reports, with informants reporting higher symptom levels than focal respondents (Gittelman & Mannuzza, 1985; Zucker et al., 2002). This finding suggests that self-report scales might underestimate the true prevalence of adult ADHD. If so, a new paradigm for assessing adult ADHD might need to be developed.

This last issue could be very difficult to address because of the practical impossibility of obtaining informant reports on adult emotional functioning in representative community epidemiological surveys other than through reports provided by spouses; this difficulty is exacerbated by the fact that a comparatively high proportion of people with adult ADHD seem to be either separated or divorced. However, this concern has been somewhat lessened by the fact that the one methodological study of adult self versus informant ADHD symptom reports carried out in a nonclinical sample found fairly strong associations between the two reports and no self–informant difference in reported symptom severity (Murphy & Schachar, 2000).

This problem is presumably greater in obtaining retrospective adult assessments of childhood ADHD, which are required for a diagnosis of adult ADHD. There is good evidence, based on prospective studies that compare adult retrospective reports with baseline evaluations made in childhood, that such retrospective reports are often inaccurate in their particulars even when they are based on clinical interviews (Shaffer, 1994). Nonetheless, it is important to note that follow-up studies show that the vast majority of adults who were diagnosed with ADHD as children retrospectively report at least some symptoms of childhood ADHD (Mannuzza et al., 2002). A more serious problem might be that a meaningful minority of adults known not to have had hyperactivity in childhood retrospectively recalled that they had childhood symptoms of ADHD (Mannuzza et al. 2002). Methodological research is needed to sort out these uncertainties and thereby improve the validity of community epidemiological studies of adult ADHD.

An important opportunity for future epidemiological research on adult ADHD lies in studies of workplace prevalence and indirect costs. The NCS-R

findings regarding the workplace costs of ADHD were remarkable: ADHD in the US labor force is associated with 120 million work loss days and an indirect human capital cost of $19.5 billion per year. Such striking results warrant further investigation. Over the past decade, employer interest in the indirect workplace costs of illness has led to a rapid expansion in epidemiological research on the prevalence and adverse workplace consequences of untreated worker health problems, as well as in cost-effective analyses from the employer perspective of targeted workplace health care interventions (Kessler & Stang, 2006). Depression has been the mental disorder of most interest to employers in this regard up to now (Stewart et al. 2003; Wang et al., 2004; Wang, Simon, & Kessler, 2003). However, if the NCS-R results are correct, then ADHD is actually more prevalent among workers than depression at any point in time; in other words, although a higher proportion of workers have depression than ADHD at some time in the year, ADHD is considerably more persistent than depression. Furthermore, the individual-level work impairments associated with ADHD seem to be greater than those associated with depression, especially among blue-collar workers. Given the recent advances in ADHD treatments that have the potential to reduce these work impairments substantially, ADHD in the workplace would seem to be an important target for future epidemiological investigation.

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Chapter 3

Gender differences in ADHD

Patricia Quinn

Introduction

The concept of ADHD – its symptoms, course, and etiology – has evolved over the years. In this process, several long-held assumptions have been set aside. Hyperactivity, once believed to be the essential feature of ADHD, is now understood to present among only a subset of those with the disorder. In addition, ADHD in adults is no longer considered merely a "residual" version of a childhood disorder, but is more accurately recognized as the adult manifestation of a life span disorder. Over the last decade another longstanding assumption has been called into question – that ADHD primarily affects males.

Gender-sensitive profiles of ADHD have been slow to develop, and although we have come a long way in the last decade toward a better understanding of the differences in manifestations of ADHD in men and women, there remains much to learn, with many avenues yet to be explored. This chapter focuses on specific issues related to ADHD in women and includes such topics as the unique presentation and the psychological effects related to late diagnosis, coexisting conditions commonly seen in women with ADHD, and the challenge of providing an appropriate treatment plan for women with ADHD.

Prevalence of ADHD in women

As ADHD in adults became more widely recognized and treated in the mid-1990s, a number of adult ADHD clinics were established. Informal reports emerging from these clinics initially suggested that the percentage of women self-referred to these clinics was much higher than the percentage of females with ADHD previously reported in the literature (Biederman, 1994; Biederman et al., 1994; Stein, 1994).

More recent studies investigating gender ratios of adults with ADHD have found that the difference in prevalence rates for males and females may diminish in adulthood (Faraone et al., 2000; Walker, 1999). Although there are no reliable data on the number of women with ADHD or the true male-to-female ratio of adults with ADHD, all of these reports strongly suggest that women with ADHD represent a more significant proportion of adults with ADHD than has been previously recognized.

Comorbid conditions in women with ADHD

It is estimated that 70–75% of adults presenting for treatment of ADHD have at least one additional psychiatric diagnosis (Shekim, Asarnow, Hess, Zaucha, & Wheeler, 1990; Wilens, Biederman, & Spencer, 2002). Although there is general agreement that gender-related differences exist in comorbid conditions, these differences have been described in clusters: boys have been found to have more "externalizing" disorders, and girls have been described as tending to have more "internalizing" disorders such as anxiety and depression. Although research on adult females with ADHD continues to lag behind that on adult males with ADHD, many clinicians are reporting unique issues and comorbid conditions in women with ADHD within their practices.

Stein and colleagues (1995) using the Wender Utah Rating Scales (WURS), conducted a factor analysis to compare self-reported symptoms of men and women diagnosed with ADHD and found significant gender differences. The responses of women in this study loaded primarily on a "dysphoria" factor, although they also reported problems with attention and organization, conduct problems, and impulsivity. In contrast,

ADHD in Adults: Characterization, Diagnosis and Treatment, ed. Jan Buitelaar, Cornelis Kan and Philip Asherson. Published by Cambridge University Press.

men's self-reported symptoms emphasized more conduct and learning problems, stress intolerance, attention difficulties, and poor social skills/awkwardness.

Anxiety and depression

Using self-report and interview data, Rucklidge and Kaplan (1997) found that women in their sample who were diagnosed with ADHD in adulthood were more apt to report depressive symptoms, were more stressed and anxious, had more external locus of control and lower self-esteem, and engaged in more emotion-oriented versus task-oriented coping strategies than women who did not meet diagnostic criteria for ADHD. Similarly in research published by Katz, Goldstein, and Geckle (1998), women diagnosed with ADHD in adulthood were found to have a greater degree of psychological distress than their male counterparts on measures of psychiatric symptoms, but displayed more efficient cognitive strategies on neuropsychological measures.

As previously cited, a study conducted by Stein and colleagues in 1995 found that the ADHD symptoms most frequently reported by women were dysphoria, inattention, organization problems, and impulsive conduct. The largest factor extracted for females was dysphoria, which was described as a reactive moodiness rather than true depression with vegetative signs. A study conducted by Arcia and Conners (1998) also found important differences between male and female responses on self-ratings: adult women had a poorer self-concept and reported fewer assets and more problems than did their males counterparts. In general, females with ADHD report emotional instability characterized by fluctuating anxiety, depression, and sudden mood swings leading to difficulty in self-regulation (J Young, 2002).

Findings recently reported from the preliminary analysis of a comorbidity study involving 3559 individuals with ADHD, ranging in age from 2 to 88 years, also confirmed an increase in mood disorders in females (Turgay et al., 2005). In the adult population only, major depression, anxiety disorders, and dysthymic disorder were the most prevalent comorbid conditions reported. In addition, women were found to have higher rates of major depression, anxiety disorders, and dysthymic disorders than men (54% vs. 36%, 28% vs. 15%, and 16% vs. 13%, respectively).

In another study, investigators highlighted differences between 188 women and 348 men, all self-referred, who participated in a multisite placebo-controlled nonstimulant drug study (Robinson et al., 2005). In comparison with male participants, the women were more likely to have combined-type ADHD and reported more ADHD, depression, and anxiety symptoms. Women also endorsed more emotional dysregulation as measured on the Wender-Reimherr Adult Attention Deficit Disorder Scale.

The gender-specific comorbidity patterns found in the two previous studies diverge from evidence obtained from large clinical studies that lifetime comorbidity rates in ADHD do not vary by gender. Those large studies found that the only gender-related difference in lifetime rates of psychiatric comorbidity were lower rates of conduct disorder and antisocial personality disorder in women than men (Biederman et al., 2004).

Low self-esteem

Research has also highlighted the fact that women with ADHD struggle with a more negative self-image than do men with ADHD (Arcia & Conners, 1998). Societal criticism of impulsive, risk-taking behavior in girls and greater maternal criticism of ADHD behavior in daughters (Barkley, 1994) often become internalized. It is this ingrained low self-regard and lack of faith in one's acceptability, rather than the cognitive challenges of ADHD, that most likely result in the greatest long-term psychological damage seen in women (Rucklidge & Kaplan, 1997).

Social isolation and withdrawal

In her book, *Women with Attention Deficit Disorder* (1995), Solden described women "coming out of the ADHD closet" as they grow in self-acceptance and self-understanding through psychotherapy. Many young girls with ADHD enter this "closet" early in life, spending childhood years anxiously avoiding class participation for fear of embarrassment. Often, these girls isolate themselves socially because of social anxiety and sometimes outright peer rejection. Some research suggests that girls with ADHD experience more peer rejection than boys and that these patterns begin as early as preschool (Berry, Shaywitz, & Shaywitz, 1985). Other studies (Brown, Madan-Swain, & Baldwin, 1991; Hinshaw, 2002) found that peer rejection of girls with ADHD begins early and tends to increase with age.