Comorbidity of Attention-Deficit/Hyperactivity Disorder With Psychiatric Disorder: An Overview

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Attention-deficit/hyperactivity disorder (ADHD) has been noted to be comorbid with a variety of psychiatric disorders. These include oppositional defiant and conduct disorders, as well as affective, anxiety, and learning disorders. Considerable debate has revolved as to the meaning of this overlap. Does it occur by chance or is it an artifact of referral bias? Are the comorbid conditions secondary to the ADHD, or can other psychiatric disorders masquerade as attentional problems? Alternatively, ADHD may exist as distinct subtypes, each with its specific comorbidity. Studies that have examined the comorbidity of oppositional, conduct, affective, anxiety, and learning disorders in ADHD are reviewed. ADHD and ADHD with conduct disorder appear to be distinct subtypes, possibly with different etiologies. While the short-term response to stimulants is the same in these two groups, children with ADHD and conduct disorder children have higher rates of antisocial personality as adults. Coexisting anxiety appears to attenuate impulsivity in ADHD, and stimulant response is poorer in ADHD children with comorbid anxiety. Anxiety and ADHD appear to be inherited independently. A subset of ADHD children also meet criteria for bipolar disorder, although the exact prevalence of this diagnosis in ADHD children is strongly debated. Regardless of prevalence, this is a severely impaired group of ADHD children, with high rates of aggression and psychiatric disorder in their families. The comorbidity of ADHD and major depression is much less studied, and few firm conclusions can be made about it. Finally, about 20%–25% of ADHD children meet criteria for a learning disorder, but learning disorders appear to be independent of ADHD. *(J Clin Psychiatry 1998;59[suppl 7]:50–58)*

It is clear from both clinical practice and epidemiologic studies that many children with ADHD have other psychiatric conditions that complicate their clinical management. Angold and Costello[1] have pointed out the various factors that might explain the overlap of comorbid disorders: (1) the overlap is in fact no greater than chance, but clinicians, particularly mental health professionals, are more likely to have complex cases present to their practices; (2) the comorbid condition is secondary to the ADHD (for instance, a child becomes depressed because of chronic school problems); (3) ADHD has a distinct genetic or environmental etiology, while ADHD with the comorbid condition has a completely separate set of etiologic factors (i.e., ADHD and ADHD with conduct disorder might have different genes); and (4) ADHD has a particular cause, but different environments cause ADHD children to take different paths, leading one group to develop the comorbid condition. Regardless of cause, comorbidity is important at a clinical level because an ADHD child with a comorbid condition may have a different clinical presentation, life course, and response to treatment than a child with ADHD alone. This paper will focus on three comorbid conditions commonly seen in clinical practice: (1) ADHD with oppositional defiant disorder or conduct disorder, (2) ADHD with affective/anxiety disorders, and (3) ADHD with learning disorders. The issue of ADHD and comorbid Tourette's disorder (as well as obsessive-compulsive disorder) is more fully addressed elsewhere.[2]

ADHD AND DISRUPTIVE BEHAVIOR DISORDERS

About half of children with ADHD will meet criteria for either oppositional defiant disorder or conduct disorder. Despite the fact that there are important distinctions between oppositional defiant disorder and conduct disorder,[3] most epidemiologic studies combine these diagnoses. Age has a distinct effect on these statistics. Almost all children under the age of 12 years who meet criteria for oppositional defiant disorder or conduct disorder will also meet criteria for ADHD.[4,5] In adolescent samples, pure conduct

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disorder is more common: only about a third of adolescent conduct disorder patients meet criteria for ADHD.[5] Many features distinguish ADHD and ADHD/conduct disorder children. ADHD/conduct disorder children come from families of lower socioeconomic status than ADHD-only children.[6] Teachers rate ADHD/conduct disorder children as having more symptoms of inattention and hyperactivity than ADHD children without conduct disorder,[4,7] although these groups are not different from each other on actual laboratory measures of activity level.[8] Laboratory measures of attention and impulsivity such as the Continuous Performance Test (CPT) or the Matching Familiar Figures Test do not distinguish these groups,[7–10] although in one study children who were both hyperactive and aggressive as rated by teachers did make more impulsive errors on the CPT than children rated as only hyperactive.[11]

In contrast to the lack of differences between ADHD and conduct disorder children in terms of laboratory measures of cognition, there are striking differences in these groups on measures of academic achievement. McGee et al.[12] found that the rates of reading disorder in the ADHD, ADHD/conduct disorder, and control groups were 19%, 36%, and 7%, respectively. Moffitt and Silva[13] compared 13-year-olds in four groups: ADHD, ADHD plus delinquency, delinquent with no history of ADHD, and controls. ADHD boys without delinquency were no different from controls on neuropsychological measures, whereas the ADHD-delinquents were impaired in terms of verbal skill, visual motor integration, and visuospatial skills. Impairments were most profound in the verbal area. ADHD children with poor verbal skills at age 3 were already showing reading problems at age 5; these children were particularly prone to delinquency as teenagers.[14]

Medical and perinatal history does not distinguish ADHD from ADHD/conduct disorder children.[4,12,14–16] Studies have consistently shown that ADHD children with conduct disorder have a much stronger family history of antisocial behavior in their first-degree relatives compared with children with ADHD alone.[6,17–19] Indeed, for children who have ADHD alone, the rate of antisocial behavior in relatives does not exceed that of control children. Biederman et al.[19] examined the rate of psychiatric diagnosis among the relatives of a large sample of ADHD and ADHD/conduct disorder children. The risk for ADHD was the same in both groups of relatives, but the ADHD/conduct disorder children had an elevated number of relatives with conduct disorder (26%) compared to the ADHD-only group (13%). Furthermore, relatives with conduct disorder also tended to have ADHD; that is, the two disorders cosegregated, indicating that ADHD/conduct disorder is a distinct familial subtype. This confirms an earlier study[15] which also found that ADHD/conduct disorder children were more likely to have siblings who suffered from both ADHD and conduct disorder, whereas the siblings of children with ADHD alone had only hyperactivity.

The long-term outcomes of ADHD and ADHD/conduct disorder children are very different. August et al.[20] followed two samples of hyperactive children, one with pure hyperactivity and the other high aggressivity. At follow-up, the subjects had a mean age of about 14 years. The hyperactive-aggressive group showed more antisocial and defiant behaviors. There were no cases of drug or alcohol abuse in the hyperactive only group, whereas 30% of the hyperactive-aggressive group had engaged in substance abuse. Loeber et al.[21] found that a third of ADHD/conduct disorder children had committed multiple crimes as teenagers, compared with only 3.4% of ADHD children without conduct disorder. While ADHD by itself conveys some risk for adult antisocial behavior, it is when the ADHD child has a comorbid conduct disorder that the risk of adult antisocial personality and criminal conviction rises sharply.[22,23]

Many studies have compared ADHD and ADHD/conduct disorder children in terms of responsiveness to stimulant medication. When stimulant is compared with placebo in double-blind protocols, ADHD/conduct disorder children show an equally robust response to methylphenidate as do ADHD children without conduct disorder.[24–26] ADHD/conduct disorder children not only show the same reductions in inattentiveness and hyperactivity as ADHD-only children, but antisocial behaviors themselves are reduced.[27] Overt aggressive behavior toward peers is clearly reduced when ADHD/conduct disorder children are taking stimulants.[28,29] Hinshaw et al.[30] found reductions in rates of stealing and vandalism when ADHD children were taking stimulants relative to placebo. Curiously, ADHD children on stimulant medication were more likely to cheat, which the authors interpreted as a result of increased task involvement. Thus, stimulants should never be withheld from the ADHD/conduct disorder child because it is assumed the child's behavior is simply willful. Lithium has been found to be superior to placebo in reducing aggressive behavior of conduct disorder in the inpatient setting[31]; most of the subjects in this study most likely had comorbid ADHD. Klein et al.[32] treated conduct disorder children, most of whom had ADHD, in a double-blind placebo-controlled study of lithium and methylphenidate. Whereas methylphenidate was clearly effective in reducing antisocial behavior, lithium was not different from placebo in this regard. Lithium has also been shown to be ineffective for ADHD symptoms per se.[33] A combined approach, using both lithium and stimulants, may be necessary in the ADHD/conduct disorder child to treat the full range of both inattentive and aggressive symptoms. With proper monitoring, these drugs can be combined safely.[34] Although it is assumed that ADHD/conduct disorder children require more intensive psychosocial intervention than ADHD-only children, no studies have addressed this issue. The multicenter Multi-Modality Treatment of ADHD (MTA) study currently underway will possibly shed some light on this issue.[35]

ADHD AND DEPRESSIVE DISORDERS

In many ways the study of ADHD and conduct disorder is made easier by the overt, specific nature of the symptoms (fighting, stealing, temper outbursts). Adults can directly observe them, and many established instruments can measure these behaviors. The same is not true for depressive and anxiety symptoms in children. Reliability of parent and child report is lower for internalizing symptoms than externalizing symptoms, in both standard[36] and research interviews.[37,38] There is no agreement on the manner in which data from parent and child interviews should be combined. For instance, the child may report he is depressed, feels guilty, and has trouble sleeping, but deny all other problems. The parent may deny the child is depressed, but report concentration difficulties and loss of appetite. Should the total symptoms from the parent and child interview be combined to yield a diagnosis of major depression? This is what is done in most clinical practices, yet each clinician has developed a different method of integrating this information. Other studies rely only on the parent report, but if a parent says the child is depressed while the child strenuously denies depression, are we making a valid diagnosis? If we use the child report, then we must examine the issue as to how children at different developmental levels express their symptoms. Evaluating depression in ADHD has added dimensions of difficulty: "Irritable mood" can be used in the place of depressed mood to make a diagnosis of affective disorder in children, but children with oppositional defiant disorder/conduct disorder are often irritable as part of their temper outbursts. Even children with ADHD alone, as part of their impulsiveness, may be emotionally labile.

Given these issues, it is not surprising that studies have yielded highly discrepant results as to how prevalent affective disorder is in the ADHD population, with estimates ranging from 3% (which is not greater than that in the general population) to as high as 75%.[39] The most well-done studies show prevalence rates of 9% to 38% for depressive disorders in ADHD children.[19,40,41] Surprisingly, no study has directly compared ADHD children with and without major depressive disorder (MDD) on specific clinical measures. Pre-DSM studies that compared "hyperactive" children to children with both "hyperactivity" and "emotional disorders" found the groups similar to each other in terms of family variables, reading disorders, CPT performance, and behavioral ratings of ADHD variables.[9,42] Depressive symptoms generally have an onset after the ADHD symptoms,[43,44] and the coexistence of ADHD and MDD does not appear to prolong the depressive episode or number of depressive episodes.[43,45,46] ADHD is not associated with an increased risk of suicide attempts or suicide completion.[47,48] It is the comorbidity of conduct disorder or substance abuse that increases the risk of suicide completion.[49]

Biederman et al.[19] examined the prevalence of both ADHD and MDD in the relatives of ADHD children with and without MDD. If the child had only ADHD, the rates of ADHD and MDD in first-degree relatives were both elevated over the rates of a control group. A similar pattern was found in the ADHD/MDD group. The fact that relatives of nondepressed ADHD probands also had an increased risk of MDD suggested some common familial links with ADHD and MDD. The disorders did not cosegregate, meaning the two disorders occurred in different relatives (i.e., an uncle with ADHD and a cousin with MDD). These findings, if confirmed, have a profound implication for the study of both ADHD and MDD, for they suggest that a common genetic factor underlies both. Some environmental factor then controls whether the individual expresses this genetic factor as ADHD, MDD, or ADHD/MDD. It should be borne in mind that these studies used primarily the parent report to make the diagnosis of MDD, and many of the ADHD children in the study were not past the age of risk for MDD. If they developed MDD in the future, this would move them (and their depressed relatives) into the ADHD/MDD group and reduce the prevalence of MDD in the relatives of the ADHD-only group.

No studies have compared stimulant responsiveness in ADHD and ADHD/MDD subgroups, nor have there been any studies of differential response of these groups to psychotherapy. It is widely assumed that antidepressants might have a particular role in treating the ADHD/MDD subgroup, given the ability of these drugs to treat the symptoms of both ADHD and depression. Desipramine, however, was found to treat ADHD alone and ADHD with depression equally well, at least in terms of ADHD symptoms.[50] It has been shown that both fluoxetine and tricyclic antidepressants can be safely combined with stimulants[51–53] to treat this comorbid subgroup. No unusual side effects were encountered in any of these studies.

ADHD AND BIPOLAR DISORDER

How prevalent is bipolar disorder in children with ADHD? This topic has generated heated controversy and has grown out of the more general issue as to how common bipolar disorder is in children and adolescents generally. Epidemiologic studies[40] have not found high rates of the disorder, although it should be noted that instruments used may not have been sensitive to the diagnosis of bipolar disorder. Two long-term follow-up studies of children with ADHD find no evidence of comorbidity with bipolar disorder in ADHD.[54,55] Early studies did show that children diagnosed as manic have a high degree of symptoms of ADHD and other externalizing disorders.[56] Recently, Wozniak et al.[57] examined 262 clinically referred prepubertal children and found 43 that met criteria for mania; all but 1 of these children also met criteria for ADHD. Within this sample, there were 164 cases of non-bipolar

ADHD; thus, the rate of mania in this sample of ADHD children was 16%. There were only 2 children with euphoric mania; 77% showed "extreme and persistent mania." Eighty-four percent showed "mixed mania" in which symptoms of mania and major depression co-occurred. Compared to non-bipolar ADHD children, the comorbid group showed a higher rate of reading disorders and lower Global Assessment of Functioning (GAF) scores. They also had higher rates of other psychiatric disorders including conduct, anxiety, and depressive disorders. Similar results emerged from a second sample of ADHD children studied by this group.[58] Child Behavior Checklist scores of manic ADHD children were elevated over those of non-manic ADHD children on nearly all subscales, but particularly on the aggression subscale. ADHD/manic children were found to have higher rates of bipolar disorder among their relatives, while the rate of bipolar disorder in the relatives of non-manic ADHD children did not exceed that of a control group.[58,59]

It seems clear that classic euphoric mania, with clear-cut cycling, is quite rare in children and adolescents. Studies of the Massachusetts General group[57,58] have noted the *persistence* of the manic symptoms, rather than any cycling. Some have argued that this violates the requirement of DSM-III-R that "distinct" periods of mania (clearly different from baseline behavior) be present.[60,61] It is agreed that a population of children exists that might be termed *ADHD-multiplex*. They show severe ADHD symptoms, aggressive outbursts, and chronic irritability. Do they in fact have bipolar disorder? Do they constitute some other variant of ADHD that will prove to be distinct from mood disorders? Following these children into adulthood to determine if they develop a more "classic" picture of bipolar disorder might be one way to resolve the issue. If a genetic marker for bipolar disorder is confirmed, one could determine if this marker is present in these ADHD-multiplex children.

In any case, clinicians do not have to wait for resolution of the scientific issue to treat these difficult cases. While lithium has not been shown to be particularly successful in small studies of bipolar children,[62] more extensive trials are underway.[63] Valproate, found to be effective in adult mania,[64] has shown promise in adolescent mania, although no controlled trials have been performed.[65] Lithium and stimulants can be safely combined in the ADHD/manic child without unusual side effects.[34] If an aggressive child responds to lithium, however, one should not view this fact alone as a validation of bipolar disorder, because aggressive children without mood disorder show improvement on lithium.[31]

ADHD AND ANXIETY DISORDERS

About a quarter of children with ADHD will meet criteria for an anxiety disorder, compared with 5% to 15% of the general population.[66] Recently DSM-IV abolished the diagnosis of overanxious disorder, which had seven specific criteria, and merged it with generalized anxiety disorder (GAD), which is a good deal more vague in its criteria. As with depression, there is debate as to whose report should be relied on for making the diagnosis, parent or child? Pliszka[67] found that half of the ADHD children who met criteria for overanxious disorder by their own report were not described as anxious by their parents, suggesting that, as with depression, parents may often be unaware of their child's internalizing symptoms. Tannock[68] compared two groups of ADHD/anxiety disorder children: one group met criteria by child report, whereas in the other group the children denied anxiety but the parent reported anxiety symptoms in the child. Only the ADHD/anxiety children who themselves endorsed anxiety showed lower levels of self confidence and impairment in daily activities. This suggests that it is the child, rather than the parent interview, which is more important in making the diagnosis of anxiety, but further research is needed to resolve the issue.

How are ADHD children with and without comorbid anxiety different from each other? Pliszka[25,67] found that children with ADHD and overanxious disorder were older at the time of presentation than children with ADHD alone. An initial study[25] found that ADHD/overanxious disorder children were less likely to meet criteria for conduct disorder and had lower teacher ratings of inattention/hyperactivity than ADHD-only children. However, when a structured interview was used in a larger follow-up study, these findings were not confirmed.[67] Biederman et al.[69] also did not find differences in the rate of conduct disorder in ADHD and ADHD/anxiety children. In contrast, Tannock[68] found higher rates of conduct disorder among ADHD/anxiety children. Neither Tannock[68] nor Biederman et al.[69] found differences between ADHD children with and without anxiety in terms of the prevalence of learning disabilities. While ADHD/anxiety and ADHD-only children were not found to be different in school performance,[69] ADHD/anxiety children reported more school problems than ADHD-only children.[70] Indeed ADHD/anxiety children reported a wide variety of social difficulties beyond those reported by children with ADHD alone. Mothers of children with ADHD/anxiety reported higher levels of problems during pregnancy and developmental delays than mothers of children with ADHD alone.[68] Children with ADHD/anxiety have generally experienced more stressful life events than ADHD-only children.[68,71] Biederman et al.[69] found much higher rates of divorce and separation among the families of ADHD/anxiety children (59%) compared with ADHD-only children (27%).

Pliszka[25,67] used the observation technique of Barkley[72] to assess the motor behavior of ADHD children with and without overanxious disorder. Children were placed in an observation room with a one-way mirror and required to

perform arithmetic while being watched by a research assistant blind to the clinical information. Children were rated in terms of off-task behaviors, fidgeting, vocalizing, getting out of their seats, and playing with objects. In both studies, children with ADHD/overanxious disorder were less likely to display these impulsive-hyperactive behaviors than ADHD-only children. The second study[67] compared both ADHD groups with controls. When the numbers of ADHD behaviors were totaled, the ADHD-only children were significantly more off task and disruptive than the ADHD/overanxious disorder children, who in turn were significantly more disruptive than the controls. The cognitive performance of ADHD children with and without anxiety has been compared using a variety of measures. Pliszka[25] used the Memory Scanning Test and found that the ADHD group had shorter reaction times than the ADHD/overanxious disorder group and a higher number of errors. This suggested that as the task became more cognitively difficult the ADHD-only children became more impulsive, whereas the ADHD/overanxious disorder children slowed their reaction times. In a follow-up study, Pliszka[67] compared ADHD children with and without overanxious disorder with normal controls on the inhibition version of the CPT. On this task, children were required to press a button every time a shape appeared on the screen; if they saw a blue square, they had to withhold their response. Children with ADHD alone had a much higher number of errors of commission than children with ADHD/overanxious disorder, who in turn were not different from normal controls.

Tannock et al.[73] examined the differences between ADHD children with and without anxiety on a working memory task. In contrast to the CPT, which involves only simple inhibition, working memory tasks require the manipulation of information. ADHD children with and without anxiety performed the Children's Paced Auditory Serial Addition Task. Subjects were presented a series of digits (i.e., 4, 5, 1, 7, etc.) by a tape recorder. They had to add the first two digits in the sequence (4 + 5 = 9). When they heard the third digit, they had to add it to the second (5 + 1 = 6); and when they heard the fourth digit, they had to add it to the third (1 + 7 = 8), and so on. The digits were presented in three different blocks of varying speeds. When the digits are presented at longer intervals, working memory is taxed because the information must be retained longer. The ADHD/anxiety children made more errors when the digits were presented at longer intervals, implying a greater impairment of working memory relative to the ADHD-only children. Reviewing the data on cognitive performance, Tannock[68] suggested that the effect of anxiety in ADHD is to decrease impulsiveness on one hand, but to increase difficulties with working memory and effortful processing. Thus, clinically, ADHD/anxiety children are more likely to appear less overtly hyperactive and disruptive, but more "slowed down" or inefficient.

Biederman and colleagues[19,69] have performed family studies similar to those reviewed in the depression chapter to explore the pattern of inheritance of ADHD and anxiety. As in the depression studies, the relatives of ADHD-only or ADHD/anxiety probands were examined for the presence of ADHD or anxiety. Compared to rates in controls, the rate of anxiety disorders was elevated only in the relatives of ADHD/anxiety children, and not in the relatives of ADHD-only children. This is most consistent with the hypothesis that ADHD and anxiety are separate disorders inherited independently of each other. The most recent family study comparing ADHD and anxiety disorder children has confirmed this pattern.[74]

On the basis of a review of the literature, Pliszka[75] suggested that children with comorbid ADHD and anxiety might show a less robust response to stimulant medications than ADHD children without internalizing disorders. Seeking to determine predictors of stimulant response, Taylor et al.[76] treated a heterogeneous group of boys with behavior problems with a double-blind placebo-controlled trial of methylphenidate. Boys who at baseline had more symptoms of depression or anxiety were least likely to respond to the drug. Pliszka[25] examined this issue by treating 43 ADHD children (13 of whom had comorbid overanxious disorder) in a double-blind placebo-controlled trial of methylphenidate. Children received a week-long placebo run-in, and then were randomized to a 3-week crossover study of placebo and two doses of methylphenidate. Teachers, who were blind to medication status, rated the children each of the study weeks. Once a week, the children returned to the laboratory where they performed arithmetic problems for 15 minutes while being observed through a one-way mirror. The observer was also blind to medication status. Over 80% of the nonanxious ADHD children were stimulant responders, while only 30% of the ADHD/overanxious disorder children were felt to clearly benefit from the drug. There were a number of placebo responders in the ADHD/overanxious disorder group, whereas there were virtually no such responders in the nonanxious ADHD group. The effects of stimulants on the observation room ratings were particularly striking. Nonanxious ADHD children had a highly significant reduction in ratings of off-task and fidgeting behaviors in response to methylphenidate, while ADHD/overanxious disorder children showed little improvement on this measure.

There was no evidence that the ADHD/overanxious disorder children suffered any unusual side effects, nor did they appear to get more anxious. Of course, 30% of the ADHD/overanxious disorder children did respond well to stimulants and continued treatment with methylphenidate; thus, the study did not show that stimulants are absolutely contradicted in ADHD/anxiety. In contrast, Tannock et al.[77] did find that side effects of stimulants appear more frequent in the ADHD/anxiety group relative to the ADHD-alone group. Furthermore, these ADHD children

were followed while they received long-term methylphenidate treatment (over 12 months). Not only did ADHD/overanxious disorder children have less behavioral improvement, but what improvement there was tended to decline over time.[68] Recently, Tannock et al.[73] compared ADHD/anxious and ADHD-only children on a working memory task. Children performed the task on placebo and several dosages of methylphenidate ranging from 0.3–0.9 mg/kg/dose. ADHD children without anxiety showed clear improvements in performance while taking methylphenidate, which linearly related to dose. In contrast, ADHD/anxious children taking the low dose showed only modest improvements, which were not enhanced by the higher dose. DuPaul and colleagues[78] divided ADHD children into internalizers and noninternalizers based on the child's baseline Child Behavior Checklist score. Similar to Pliszka,[25] they found that ADHD children with comorbid internalizing symptoms had a less robust response to stimulants than nonanxious ADHD children. Buitelaar et al.[79] also found low anxiety to predict a good stimulant response in an unselected group of ADHD children.

ADHD AND LEARNING DISORDERS

Learning disorders are defined in various ways. In the first method, there is a discrepancy between the child's IQ and his performance on a standardized test of achievement. Research studies vary as to whether the child must be 1.5 or 2.0 standard deviations below the score predicated by his IQ to be classified as having a learning disorder, and this can affect prevalence levels (Table 1). Alternatively, a combined approach can be used: the child's achievement score must be more than 1.5 standard deviation below the level predicted by IQ, and the absolute standard score on the achievement test must be below 85. This is a more conservative approach, but may underidentify highly intelligent persons with learning disorders. As noted by Barkley[72] when more liberal criteria are applied, 40% to 60% of ADHD children are identified with a learning disorder, but using more rigid standards, about 20% to 30% of ADHD children will be learning disabled in the area of reading, spelling, or arithmetic.

How are ADHD and ADHD/learning disorders children different from each other? Most of the research had been conducted on ADHD children with comorbid reading disabilities. When ADHD children with good reading ability are compared with ADHD/reading disabilities children, there is very little overlap of symptoms. That is, ADHD children are impaired on measures of impulse control, but perform as well as controls on phonological tests. Conversely, dyslexic children whose Conners ratings are in the normal range do well on attentional tests but perform poorly on language measures, confirming that ADHD and reading disabilities are distinct entities.[87–89] ADHD children with and without reading disabilities did not differ from each other in severity of hyperactivity, aggression, or anxiety.[83] Both ADHD and reading disabilities have strong genetic components, but appear to be inherited independently.[86,90–93]

Table 1. Overlap of Learning Disorders in Attention-Deficit/Hyperactivity Disorder

Study	Method	Reading	Spelling	Arithmetic
McGee et al[12]	IQ Discrepancy			
	Hyperactivity	19%		
	Hyperactivity + conduct disorder	37%		
August and Holmes[80]	IQ Discrepancy			
	Hyperactivity	7%		
	Hyperactivity + conduct disorder	8%		
Dalby[81]	IQ Discrepancy			
	ADHD	9%		
Shaywitz and Shaywitz[82]	IQ Discrepancy			
	ADHD	11%		
Halperin et al[83]	Combined			
	Hyperactivity	9%		
Barkley[72]	IQ Discrepancy	41%	60%	60%
	Achievement score only	21%	26%	29%
	Combined	19%	24%	26%
Dykman and Ackerman[84]	Combined			
	ADHD	53%		
	ADHD/conduct disorder	34%		
	ADD	37%		
Frick et al[85]	IQ Discrepancy	16%		21%
	Combined	8%		12%
Semrud-Clikeman et al[86]	IQ Discrepancy[a]	38%		55%
	IQ Discrepancy[b]	23%		30%
	Combined	15%		33%

[a]Wide-Range Achievement Test score > 10 standard score points below full scale IQ.
[b]Wide-Range Achievement Test score > 20 standard score points below full scale IQ.

In terms of treatment, children with reading disabilities alone do not show increased reading skills when treated with stimulants,[94] but ADHD/reading disabilities children do show increases in reading achievement test scores when their inattentiveness is successfully controlled with methylphenidate.[95] ADHD and ADHD/reading disabilities children also show an equally robust behavioral response to stimulants.[84] No studies have been done comparing reading disabilities–only children and ADHD/reading disabilities children in response to special tutoring or remedial education. Although the above studies do suggest that if the ADHD child's inattentive symptoms are not controlled, such remedial work may not be as successful as in the treated child. Studies are needed of the comorbidity of ADHD with other types of learning disorders such as mathematics or spelling disorders.

CONCLUSIONS

A rich body of data has emerged showing the heterogeneity of ADHD and its association with other psychiatric disorders. ADHD/conduct disorder clearly appears to be a

distinct subtype, and while it responds well to stimulants in the short run, the long-term course is quite stormy. It may prove to have a distinct genetic etiology from ADHD alone. Anxiety disorders, in contrast, seem to be independent of ADHD and simply co-occur with it. When ADHD children are anxious, they show lower impulsiveness, although they are still impaired on this dimension relative to controls. Their response to stimulants is clearly poorer than that of children with ADHD alone, and alternative agents such as antidepressant medications may need to be considered. The pattern with mood disorders is much less clear, and further research is needed to look at how prevalent bipolar disorder is among ADHD children. As with anxiety disorders, learning disorders are independent of ADHD and simply co-occur. Children with the "triple comorbidity" of ADHD, conduct disorder, and reading disabilities may be particularly likely to show antisocial behaviors as adults. From both the clinical and research perspective, the comorbidity of psychiatric disorder with ADHD needs to be taken into account. With advances in molecular genetics and neuroimaging, it should be possible to elucidate the relationship of ADHD to its comorbid conditions.

Drug names: desipramine (Norpramin and others), fluoxetine (Prozac), methylphenidate (Ritalin).

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