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ADHD Expert Column Series

Depression and ADHD: What You Need to Know

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Introduction

The historical evidence for the basis of major depressive disorder as a disease dates back thousands of years. Even the father of medicine, Hippocrates, described melancholia as a distinct disease entity. The history of attention-deficit/hyperactivity disorder (ADHD), however, is much more recent, dating back about a century. In part, this "delay" was the result of misidentification of ADHD because the symptoms fit smoothly into the wide spectrum of human behavior. Although it is possible to find individuals who have never experienced a major depression or a suicidal thought, it is much less likely to find someone who has never felt distracted, disorganized, or impulsive at least at some point in their lives. The context of today's fast-paced society makes this even more pertinent. True ADHD, then, is a disorder of severity, chronicity, and impairment.

George Still first mentioned the condition we now know as ADHD in 1902 in *The Lancet*,^[1] when ADHD was thought to be a hyperactive disorder of childhood. Only later was it discovered that this disorder encompasses a constellation of symptoms including inattention and impaired impulse control. The understanding that a percentage of childhood cases of ADHD persist into adulthood came much later, with the DSM-III-R^[2] in 1987. While the existence and burden of adult ADHD have previously been questioned, ample data now support the validity of ADHD as a diagnosis.^[3] Such well-known individuals as James Carville^[4,5] (political consultant), David Neeleman^[6] (founder of JetBlue Airways), and Scott Eyre^[7] (pitcher for the Chicago Cubs) have publicly acknowledged that they have ADHD as adults.

ADHD and Depression

ADHD and major depressive disorder (MDD) are among the most common psychiatric disorders occurring in adulthood. The National Comorbidity Survey-Replication data show a lifetime prevalence for MDD of more than 16%, greater for women than for men.^[8] The 12-month prevalence was 6.7%. The same survey found current clinically significant ADHD in adults in 4.4% of the sample population, with a higher prevalence in men than in women. When one considers

that ADHD is under-recognized and undertreated in adults,^[9] it is easy to see that ADHD may be surreptitiously complicating the treatment of myriad psychiatric disorders.

There was early speculation that a connection between depression and ADHD must exist. Several studies, including the National Comorbidity Survey, have now demonstrated this connection ([Table 1](#)).^[8,10] Among respondents who met criteria for a 12-month prevalence of MDD, 9.4% also met criteria for ADHD. Inversely, of respondents who met criteria for ADHD, 18.6% of them also met criteria for MDD within the previous year. Even more interesting, if we include dysthymia, which is a milder but more chronic depressive disorder, the percentages are larger. Of individuals who met criteria for dysthymia, 22.6% also met criteria for ADHD. Conversely, of those who met criteria for ADHD, 12.8% met criteria for dysthymia.^[10] Put in simple terms, these comorbidity data tell us that if individuals with ADHD were found to have a depressive disorder, it was more likely to be MDD. However, of all individuals found to have depressive disorders, those with dysthymia were more likely to have ADHD.

This 2-way connection between ADHD and depressive disorders has also been demonstrated in multigeneration studies that suggest a possible genetic link. Evidence shows that the incidence of ADHD in offspring of adults with recurrent depression is higher than in the general population, and that first-degree relatives of juveniles with ADHD show higher rates of MDD.^[11,12] We know that mood disorders are highly heritable; similarly, ADHD is one of the most heritable psychiatric disorders, estimated at 80%.^[13]

Alpert and colleagues^[14] performed the largest and most specific study concerning the comorbidity of MDD and ADHD. They examined 116 adult outpatients who sought treatment for major depression at an outpatient clinic. They found that 16% of the sample met lifetime diagnostic criteria for ADHD (those who met criteria for subthreshold symptoms, ie, 5-7 qualifying symptoms rather than the required 8, were also included in this group). If the criteria were strictly adhered to, 8% of the sample met criteria for both childhood and adult ADHD diagnoses. Of interest, all individuals who qualified for full childhood ADHD experienced persisting symptoms into adulthood, either at a full or subthreshold level. Only a portion of the group who met criteria for *subthreshold* ADHD as children experienced a resolution of symptoms with age.^[14] When these figures are compared with the best estimate for established prevalence of adult ADHD in the general population (4%),^[15] the rates of patients with comorbid depression are significantly higher. Furthermore, the rates of comorbidity may have been understated by Alpert and colleagues because of exclusion of participants with other comorbidities, especially personality disorders and substance use disorders. Although this comorbidity between ADHD and MDD was found to be clinically significant, the effect of ADHD on the length, severity, or response of depression was not. From these lone data, MDD behaved no differently in those with comorbid ADHD vs those without.^[14]

Which Comes First?

True causality is a difficult conclusion to reach, no matter which disease comorbidity is being discussed. Early hints at some direction, however, were presented in a study of adolescent boys who were assessed for a period of years, up to the age of 18.^[15] The findings show that ADHD predicted a later diagnosis of oppositional defiant disorder (ODD), which, in turn, predicted later anxiety and depression.^[15] On a practical level, this makes sense. Children with ADHD have

difficulty conforming to social and scholastic norms, which may cause them to act out or use other externalizing behaviors. Doing so, however, causes further social isolation and scholastic dysfunction, which can ultimately trigger anxiety and/or depressive symptomatology. This may shed some light on the comorbidity of ADHD and MDD in adults, as well as ADHD co-occurring with several other adult psychiatric diagnoses.

Evaluating ADHD and MDD

The evaluation and diagnosis of ADHD in adults have been covered in depth in previous articles. Unfortunately, no reliable objective test exists to diagnose either MDD or ADHD. However, this situation is similar for many diagnoses throughout the field of medicine. What is required is an astute clinician performing a thorough medical and psychiatric evaluation, physical exam, and diagnostic tests when indicated. Useful tests can include urine drug screening, serum TSH, complete blood count, and chemistry panel. History of central neurologic illness, infection, or trauma is also relevant. Furthermore, many common medications may directly contribute to myriad psychiatric symptoms, including those mimicking MDD and ADHD.

Because some symptoms of ADHD and MDD overlap (inattention, memory difficulties, procrastination/low motivation, irritability, and restlessness), comorbid presentations may be confusing, even to an experienced clinician. The primary factor in establishing these comorbid diagnoses is the presence of chronic ADHD symptoms since childhood, looking especially for symptoms in the absence of a major depressive episode.

Validated symptom rating scales can be used to make the diagnosis and assess the effectiveness of treatment. The Hamilton Rating Scale for Depression^[16] and the Montgomery-Asberg Depression Rating Scale are both useful tools^[17]; another useful instrument, the Beck Depression Inventory, has the advantage of being a self-report form.^[18]

For ADHD, the Adult ADHD Clinical Diagnostic Scale v. 1.2 (ACDS) and the Conners' Adult ADHD Diagnostic Interview for the DSM-IV (CAADID) can aid in diagnostic evaluations; the Adult ADHD Investigator Symptom Rating Scale (AISRS) and the Attention-Deficit Hyperactivity Disorder Rating Scale (ADHD-RS) are useful for tracking symptoms and treatment progress. The advantage of using the ACDS or AISRS is that they include modular probes and prompts that are geared to help the clinician adequately establish the breadth and impairment of adult ADHD symptomatology. Self-report symptom scales include the Adult ADHD Self-Report Scale (ASRS) and the Conners' Adult ADHD Rating Scale-Self: Short (CAARS-S:S).^[19]

Compared with other chronic and disabling disorders, ADHD is fairly prevalent in the population. Nonetheless, it appears to be greatly under-recognized and undertreated in the medical and psychiatric communities. Adler and colleagues^[9] reviewed healthcare claims data during a period of 12 months and found that the treatment of ADHD falls far short of the estimated prevalence; ADHD was diagnosed in no more than 2.5% of patients who were treated for either bipolar disorder, MDD, or an anxiety disorder. The actual prevalence estimates for comorbidity are multitudes higher than this number, as noted.^[8]

Efficacy of Treatment

Antidepressants and ADHD

At no other time in history has the acceptance and efficacy of treatment for both MDD and ADHD been so great. More than a dozen US Food and Drug Administration (FDA)-approved medications are available for the treatment of depression. Some of them also may have moderate efficacy for treating ADHD. In fact, 1 advantage in treating this comorbidity is that the treatments can overlap. An early tricyclic antidepressant, desipramine, has shown efficacy for both ADHD and MDD.^[20,21] Another, more recent option for both disorders is bupropion, a norepinephrine reuptake inhibitor (NRI).^[22,23] Other antidepressants may provide similar efficacy, such as the serotonin-norepinephrine reuptake inhibitor (SNRI) class of antidepressants, which includes venlafaxine and duloxetine. An open-label study in 1995 found that among 12 patients, venlafaxine decreased ADHD symptom ratings by half.^[24] Another open-label study from 1996 showed that 7 of 9 patients responded well to venlafaxine at a dosage of 75 mg per day.^[25] Further studies are needed using randomized and controlled methodology.

A newer norepinephrine reuptake inhibitor, atomoxetine, entered the market as a FDA-approved treatment for ADHD in adults.^[26] The clinical trials have not shown substantial effects on depressive symptoms, although the patients had not been diagnosed with major depression. However, in 1 study involving children and adolescents, treatment with atomoxetine improved both anxiety and depressive symptoms in subjects with these comorbid symptoms, though data were not found in a placebo-controlled fashion.^[27] No evidence supports the use of purely serotonergic drugs such as fluoxetine, paroxetine, sertraline, or escitalopram for the core symptoms of ADHD.

Psychostimulants and Depression

The most commonly used pharmacologic treatment for ADHD has long been the classic psychostimulants, primarily used in children. Data on adult management of ADHD are just beginning to emerge as identification and treatment of adult cases grow. Psychostimulants include the various formulations of methylphenidate (MPH), including the recently approved transdermal system (patch), and dextroamphetamine. Only 2 of these are FDA-approved for use in adults with ADHD: mixed amphetamine salts extended release (MAS XR) and dexamethylphenidate XR. The psychostimulants have been shown to be highly efficacious for ADHD in children, adolescents, and adults.^[28]

We have long known that the stimulants provide another tool in the armamentarium of treatment for major depression, especially in specialized situations or refractory patients.^[29] Even Sigmund Freud reveled at the efficacy of cocaine, an illicit psychostimulant, as an antidepressant. His only study of the drug was on himself, finding that it lifted his mood and boosted his energy.

Psychostimulants + Antidepressants

Employing a medication regimen involving both psychostimulants and antidepressants is fairly straightforward. SSRIs combined with psychostimulants can be safe and effective, with little potential for drug-drug interactions. Combining psychostimulants with serotonergic-noradrenergic reuptake inhibitors (SNRIs) or selective noradrenergic reuptake inhibitors (NRIs) can also be successful, taking care to monitor sympathomimetic side effects, which are present with both classes of drugs. Finally, combining atomoxetine with certain antidepressants can be complicated by its metabolism through the cytochrome P450 enzyme system (2D6), and would require dose adjustments when used with agents such as fluoxetine and paroxetine.

Psychotherapy

Psychotherapies, especially cognitive-behavioral therapy (CBT) and interpersonal therapy, have a proven efficacy for treating MDD that is comparable to that of pharmacologic medications.^[30,31] A recent study using CBT as an adjunct to medication has shown promising results in adults with ADHD.^[32] Although no studies have examined interpersonal therapy for patients with ADHD, it may be effective, considering the interpersonal strain that ADHD can cause on relationships.

Psychotherapeutic interventions for ADHD in children have been successful. One study, the Multimodal Treatment of ADHD (MTA Study; [Table 2](#)),^[33] looked at rates of attaining an "excellent" response (ADHD scores in the normal range). Significant effects were seen with MPH alone, with some additional benefit with adjunctive behavioral therapies. Early results in studies of adults seem to be consistent with these data on children.

Patient Education

Psychoeducation appears to be at the heart of the success of any therapeutic intervention. Education about the neurobiological basis of ADHD can be invaluable to an adult who has long attempted to overcome what he or she perceives to be personal shortcomings. Finally, personal coaching can be used to help an individual set and achieve goals by providing strategies and encouragement along the way.

MDD takes a toll on our society. It costs the economy nearly \$40 billion annually in lost economic productivity and is estimated to be responsible for the loss of thousands of lives a year through suicide.^[34,35] Similarly, it has been shown that adults with executive function deficits (seen much more commonly with ADHD than with control subjects) have a significantly lower socioeconomic status than adults without these deficits.^[36]

Untreated ADHD can also have serious consequences that can interfere with lives, cause significant dysfunction, and increase stress, which in turn can serve as triggers for mood or anxiety disorders. Although ADHD differs from MDD in that it is always lifelong and more often ego-syntonic (assuming an innate sense of "normal" as opposed to "abnormal"), thereby evading diagnosis and treatment, its impact can be just as devastating. Suicide can be seen as a dramatic and direct result of major depression, but the morbidity and mortality associated with adult ADHD may not be as clearly evident. For example, ample data suggest that ADHD in children predicts not only higher rates of smoking in adolescents but also an earlier age of onset of smoking.^[37] Studies on adults have found higher rates of smoking for both men and women with ADHD, as well as lower rates of smoking cessation.^[38] Although no study has demonstrated higher mortality risk for adults with ADHD through higher rates of cigarette smoking, such a reasonable conclusion could be inferred in the absence of data. Untreated ADHD has also been linked to a risk of inferior school performance, lack of college completion, poor job performance, and more motor vehicle accidents.^[39-41]

Treatment for adults with ADHD can have dramatic results. Psychostimulants have efficacy rates (when dosed properly) comparable to those seen in children, in the vicinity of 70%.^[28,42] Because response rates are high and results are often seen quickly, the diagnosis and treatment of adult ADHD can be favorable for both the clinician and the patient. A cost assessment of treating ADHD compared with other chronic conditions found that treatment of ADHD in a sample

of privately insured patients was much less expensive than treating diabetes or major depression, and its cost was on par with that of the treatment of seasonal allergies.^[43]

Primary care clinicians are now on the front lines of diagnosing and treating MDD in America. They are beginning to face the same challenge with adult ADHD. Due to previously unrecognized rates in the population, the chronic nature of the disorder, and the resulting occupational and personal dysfunction, this challenge will only grow in the years to come. Proper education about and screening for both MDD and ADHD by primary care providers will continue to be imperative for the mental health of our society. The outlook is good, however, because treatment for adult ADHD comes at a relatively low annual cost, does not require inpatient treatment, yet has the potential to greatly increase functioning and improve the human condition.

Table 1. Comorbidity of ADHD

DSM-IV Diagnosis	Prevalence Rates (%) of ADHD Within Psychiatric Populations^[8]
Bipolar Disorder	21.2
Major Depression	9.4
Dysthymia	22.6
Generalized Anxiety Disorder	11.9
PTSD	13.4
Panic Disorder	11.1
Alcohol Dependence*	11.1
Drug Dependence*	25.4

*Those qualifying for a diagnosis of alcohol or drug abuse were in separate categories.

Table 2. MTA Study

	Subjects Achieving "Excellent" Response (%)
Community-based treatment-as-usual	25
Behavioral therapies alone	35
Methylphenidate alone	55

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