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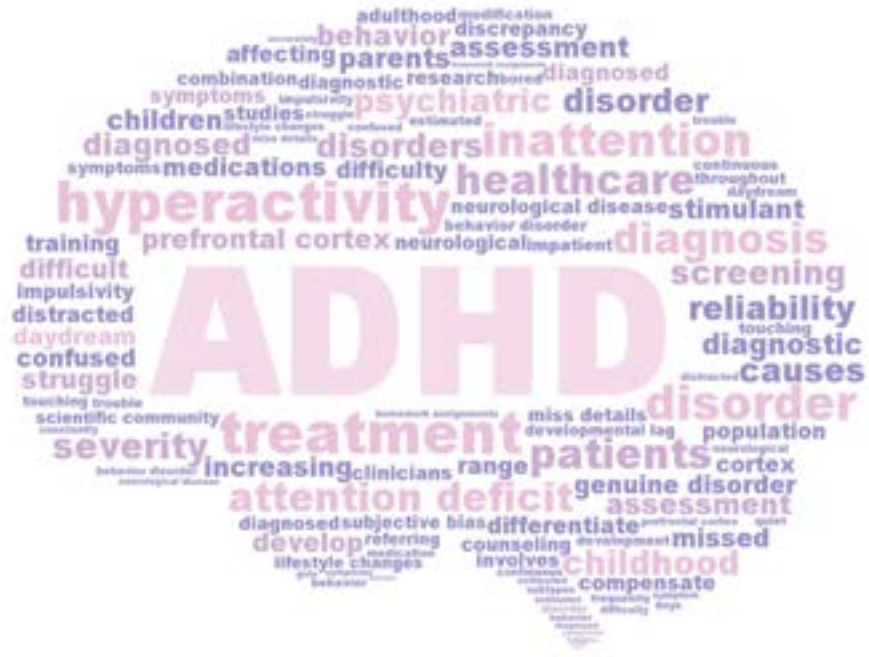

This issue of the *Residents' Journal* features articles on the theme of attention deficit hyperactivity disorder (ADHD). Arshya Vahabzadeh, M.D., discusses the implicated involvement of the dopaminergic system in the presentation of ADHD. Lauren S. Albin and Max Adelman outline the diagnosis, implications, and management of comorbid ADHD and oppositional defiant disorder. Htet Htet Linn, M.D., and Neeraj Shukla, M.D., provide data on working memory deficits in ADHD. Ahmed R. Khan, M.D., and Jeffrey W. Chenb, M.D., present information on off-label pharmacologic treatments for ADHD. Justine Wittenauer, M.D., and Caitlin D. Baptiste and Erica J. Colvin focus on treatment of ADHD in substance use disorders. Karim Sedky, M.D., presents a case report on dyskinesia that developed after mixed-amphetamine salts initiation. The issue concludes with a book review by Justine Wittenauer, M.D., of *Delivered from Distraction: Getting the Most Out of Life with Attention Deficit Disorder*.

Editorial

New Year's Resolutions

Monifa S. Seawell, M.D.
Editor-in-Chief

In the life of many trainees, July 1st marks the beginning of a new academic year. Much like the calendar New Year of January 1st, the academic new year represents a time of change and transition. As such, it may precipitate a broad emotional experience, such as a jovial celebration of accomplishments or gains, a deep internal reflection on challenging or memorable experiences, and anxiety or excitement associated with transitioning to a higher level of training and assuming greater responsibility. Many trainees also usher in the academic new year by making academic new year's resolutions or commitments toward progressing in one or more professional areas.

As is true for many of you, my academic new year has brought forth several major changes. I have graduated from general psychiatry residency to a fellow in forensic psychiatry and have advanced from the position of Associate Editor of the *Residents' Journal* to Editor-in-Chief. Both of these transitions have been associated with many of the aforementioned emotional experiences. And, like many of you, I have begun this new scholastic term by identifying opportunities for growth and forming my own academic new year's resolutions.

July 1st also marks the beginning of a new academic year at the *Residents' Journal*. The editorial staff has noted the many gains the Journal has made, identified opportunities for improvement, and developed resolutions. We look forward to implementing these over the course of the next 12 months and believe they will further enhance our Journal. I encourage you to reflect upon what you think the Journal has done well this past year, as well as any potential areas for further development. Your feedback is invaluable to us.

I also encourage you to reflect upon your own experiences over the past academic year. Congratulate yourself for things you have done well and accomplishments you have made. As you move toward identifying future opportunities for growth, I encourage you to make becoming, or remaining, involved with the Journal one of your academic new year's resolutions. At the *Residents' Journal*, we are committed to the education of trainees and to fostering authorship among medical students, psychiatric residents, and fellows. We hope that the Journal will be an important component of your year.

If you will be completing your residency this year, we would like your help in recruiting new subscribers by encouraging an incoming resident or fellow to subscribe to our monthly e-publication. Also, if you'd like to continue receiving e-mail notification alerts when each issue of the AJP Residents' Journal is published, send your new e-mail address to ajp@psych.org with the subject line "New e-mail address post-residency."

Attention Deficit Hyperactivity Disorder: Research Challenges and the Dopamine Hypothesis

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Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric disorder with a worldwide prevalence among children of approximately 5% (1). With a similar prevalence rate among U.S. adults, ADHD is one of the most common psychiatric disorders. A plethora of research has demonstrated many biological correlates; unfortunately, correlation does not demonstrate causation. While dopaminergic dysfunction is theorized to be central to this disorder, there are many challenges encountered when attempting to identify the etiology (2). A body of evidence has supported the dopaminergic dysfunction theory, including dopaminergic hypoactivity during neuroimaging, genetic associations with dopamine receptors and the dopamine transporter, and dopaminergic activity of stimulant-based ADHD treatments. Despite the hegemonic focus on dopamine, we should be cognizant that the etiology of ADHD is likely influenced by a range of gene-environment interactions. Correlations between ADHD and other monoaminergic neurotransmitters in addition to viral infections, endocrine disorders, prematurity, and nutritional deficiencies have also been noted (3). The present article focuses on several lines of evidence implicating the involvement of the dopaminergic system in the presentation of ADHD.

Symptom Heterogeneity in ADHD

Developmentally inappropriate levels of motor hyperactivity, impulsivity, and inattention characterize the core symptoms of ADHD. The symptoms lead to a demonstrable impairment in functioning. However, clinicians must depend on their own experience and expertise to determine what is "inappropriate" or "excessive" behavior. Inattention, impulsivity, and hyperactivity can be developmentally normative and may also reflect aberrant clinical symptoms of another medical or psychiatric disorder. The clinical diagnosis of ADHD is achieved through meeting criteria as outlined in DSM-IV (3). ADHD is subdivided into three symptomatically delineated subtypes, namely inattentive, hyperactive, and combined types. While ADHD is defined by 18 symptoms across two symptom domains, namely inattention and hyperactivity/impulsivity, only six total symptoms are required to establish symptomatic criteria

It is therefore important to note that a diverse constellation of symptoms may fulfill the symptom criteria for ADHD. Furthermore, it is not inconceivable that this diagnosis, with its symptomatic variability, may encompass a heterogeneous umbrella of etiologic processes. The lack of a homogenous clinical population is only one of the challenges that obstruct attempts to uncover the causative processes of the disorder, and additional barriers include limitations in our comprehension of the developing brain and gene-environment interactions.

The limitations of conducting research on diagnostic criteria defining ADHD has not been lost to researchers who acknowledge the elusiveness of clear biological mechanisms. There is no laboratory test that is diagnostic for ADHD, and it has been difficult to develop animal models. DSM-IV clinical symptoms, such as "often leaves seat in classroom" (hyperactivity) or "often does not seem to listen when spoken to directly" (inattention), require creative thinking in order to translate into animal models. However, rodent models do exist. These models include the spontaneously hyperactive rat model, an inbred strain that demonstrates locomotor hyperactivity and some abnormal responses to reward when compared with control rats (4). Unfortunately, while rodent models may provide interesting insights, their ability to fully reflect a complex human clinical condition such as ADHD has been understandably questioned.

Some researchers have used neurological testing to identify specific cognitive domains that are discordant in children with and without ADHD. Areas identified by Nigg (5), for example, highlight pronounced deficits in working memory, response suppression, attention, and reward processing. Identification of more specific impairments in these skills may allow us to develop new constructional models of ADHD, possibly endophenotypes, which may give rise to more homogenous study populations with which to continue research.

Reward Processing in ADHD

Impaired reward processing in ADHD can be demonstrated by lowered ability to tolerate delays in reward, rapid discounting of the value of delayed rewards (6), and greater impulsive choices in delay-of-gratification paradigms (7). Animal models have suggested that midbrain dopaminergic projections, in particular those from the substantia nigra pars compacta and ventral tegmental areas, are strongly correlated with reward processing (8). It has been proposed that this ventral-striatal pathway may be linked to the reward processing alterations observed in ADHD (9). Studies using functional MRI have investigated brain activation in response to both immediate and delayed rewards in individuals with ADHD and healthy comparison subjects. A relative hypoactivation of the ventral-striatal pathway is evident in ADHD (10, 11). Positron emission tomography has demonstrated that individuals with ADHD display significantly reduced dopamine transporter density and dopamine (D_2/D_3) receptors in the midbrain and nucleus accumbens (12). Interestingly, inattention, a core symptom of ADHD, has been correlated with the degree of reduction in dopamine transporter density and D_2/D_3 receptors (12).

Dopamine-Related Genetic Associations

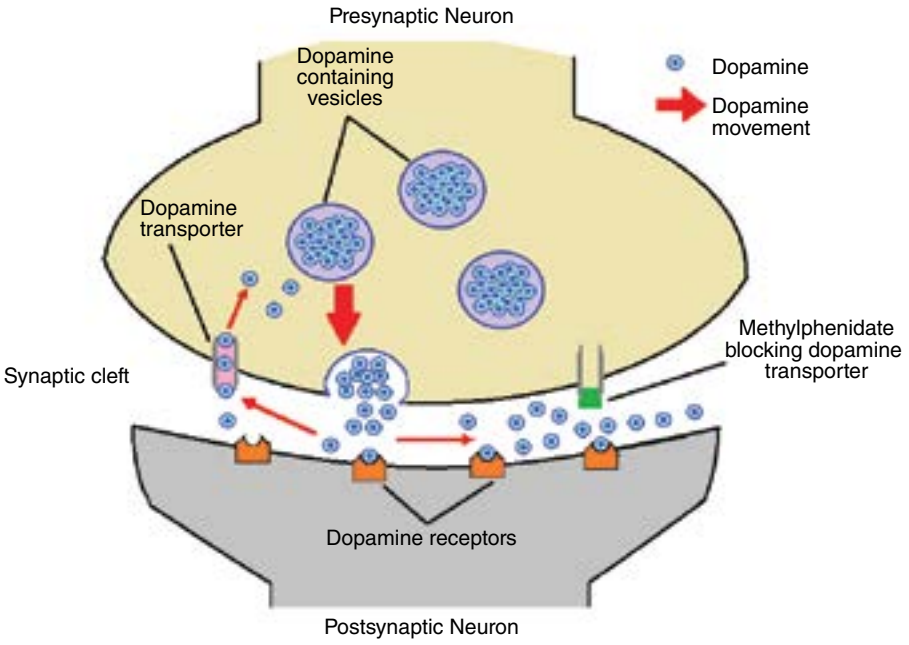
The highly heritable nature of ADHD has been established in family, twin, and adoption studies. This has prompted considerable interest in exploring the genetic basis of the disorder. Several genes with dopaminergic associations have been shown to have a statistically significant association with ADHD. These genes include the dopamine D_4 and D_5 receptors and dopamine transporter genes, in addition to the dopamine beta-hydroxylase gene (13).

The dopamine transporter is encoded by the *DAT1* gene. Interestingly, the *DAT1* gene contains polymorphisms that demonstrate a variable length, which alters the production of the transporter. This variable length is attributed to a variable number of 40 base pair repeats, referred to as a variable number tandem repeat. The variable number tandem repeat is not thought to exist at a coding site for the dopamine transporter, but rather it is thought to influence expression of the dopamine transporter protein. In vitro studies have reported that a *DAT1* allele with 10 variable number tandem repeat copies resulted in 50% greater dopamine transporter density than an allele with only nine variable number tandem repeat copies (14). While there has been some limited evidence that individual response to stimulant medication may be associated with dopamine transporter polymorphisms, disparate findings have been reported by a variety of methodologically incongruous studies, with inharmonious outcome endpoints.

Studies have also suggested that complex gene-environment interactions involving *DAT1* gene polymorphisms may increase the risk of ADHD. In one study, children were at significantly increased risk for developing ADHD symptoms if they had a *DAT1* polymorphism and were also exposed to prenatal smoking, while neither factor demonstrated significance in isolation (15). Similar findings have been reported for *DAT1* polymorphisms and prenatal alcohol use (16).

The D_4 receptor gene has been linked to ADHD through its own distinct polymorphisms. The presence of a 48-base pair variable number tandem repeat has been reported to be responsible for altered gene length. In particular, the 7-repeat variant of the D_4 receptor gene (*DRD4-7R*) has been strongly associated with ADHD (13). A recent meta-analysis of related studies demonstrated relatively higher associations between *DRD4-7R* and combined subtype ADHD compared with inattentive subtype ADHD (17). The authors excluded the hyperactive subtype because of concerns about poor temporal diagnostic stability and low prevalence. It was suggested that the findings may indicate that ADHD subtypes may in fact be separate disorders.

FIGURE 1. Conceptualized Action of Methylphenidate on the Dopamine Transporter



Psychopharmacological Support

Stimulant-based medications have been the mainstay of ADHD treatment. Stimulants possess a principal action of dopamine transporter inhibition. The dopamine transporter is the main mechanism for removal of extracellular dopamine from the synaptic cleft (Figure 1). Oral methylphenidate has been shown to block more than 50% of the dopamine transporter when administered at doses of 0.3 mg/kg–0.6 mg/kg. The time to peak behavioral effects of methylphenidate is similar to the time to peak brain uptake (18). The marked effectiveness of stimulant medication for ADHD has provided collaborative evidence for the involvement of dopamine in the etiology of the disorder. Newer nonstimulant medications, such as atomoxetine, have also demonstrated symptom reduction. Atomoxetine works specifically on norepinephrine reuptake and does not have any significant action on dopamine receptors or the dopamine transporter (19). While this observation seems to contradict the dopamine hypothesis, it has been reported that atomoxetine indirectly increases dopamine levels in the prefrontal cortex (19). The norepinephrine transporters play a substantive role in removing extracellular dopamine in this area.

Future Directions

ADHD is a highly prevalent psychiatric condition that poses many challenges to researchers in the field. The dopaminergic hypothesis is a prominent theory, which seeks to explain the etiology of the disorder. Unfortunately, while progress is

being made, it is likely that we are not attempting to identify an etiology but rather a multitude of etiologies. Further research would benefit from the identification of a more homogenous patient population, and development of endophenotypes would help to achieve this goal. While this article outlines several lines of research delineating dopaminergic dysfunction, a myriad of other neurobiological and environmental factors have been implicated. It is important that we invest our resources and time in exploring these other factors as we attempt to identify the etiology of ADHD.

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Comorbid ADHD and Oppositional Defiant Disorder: Diagnosis, Implications, and Management

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The presence of comorbid attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) in children can present unique challenges to physicians. Studies that focused on children growing up in the 1990s revealed that one in six would be diagnosed with a psychiatric disorder during childhood and one in three would exhibit multiple disorders (1) by 16 years of age. In particular, ADHD and ODD are notably prevalent, both independently and as comorbid disorders. The Centers for Disease Control and Prevention estimated that the lifetime prevalence of ADHD in children and adolescents ages 4–17 years was 7.8% in 2005, while assessments of ODD prevalence have ranged from 1.6%–10.2% in community samples (2, 3). Several studies have assessed the prevalence of ADHD with comorbid ODD, with estimates ranging widely from 15%–65% in youths between 6 and 17 years old. Most reports indicate rates close to 50% (4).

Similarities in presentation between ADHD and ODD may hinder accurate diagnosis in children with dual symptoms, and the effect of subsequent mismanagement can have far-reaching implications for childhood functionality and future adult success. It is therefore important to correctly identify cases of these disorders and to understand the clinical consequences of comorbidity on the course of treatment and management of patients presenting with both ADHD and ODD.

Overview of ADHD and ODD

ADHD is a developmental disorder defined by varying degrees of inattention, hyperactivity, and impulsivity. DSM-IV subdivides diagnoses into three subtypes: predominantly inattentive type, predominantly hyperactive-impulsive type, and combined type (5). DSM-IV criteria for diagnosing ADHD and ODD are summarized in Table 1. Increasingly, evidence suggests that ADHD is frequently comorbid with other psychiatric and developmental disorders, an observation that has profound implications for diagnosis and management of symptoms.

ODD is a disruptive behavior disorder characterized by hostile and defiant behavior and is commonly diagnosed in children with underlying ADHD. Particular risk factors for the development of ODD have been identified in a number of studies and include social and environmental factors such as, but not limited to, poverty, psychopathology in parents, poor parental monitoring, and living in a violent or disadvantaged neighborhood (4). Similarly, specific patterns of behavior beyond those generally outlined in DSM-IV criteria are excellent predictors of eventual development of ODD, both independently and in addition to existing ADHD. Persistent late-childhood physical fighting, nonimpulsive aggressive behavior, and increasing severity of aggressive behavior have been identified as possible examples of such predictive behaviors (4). To assess these behaviors, collateral information from parents, teachers, and other caregivers should be elicited, along with a thorough social and family history.

Epidemiological Patterns

Specific epidemiological patterns have also been observed in ADHD/ODD comorbidity, with gender differences especially prominent. Overall, girls were found to have lower rates of independent ODD and ADHD; however, after controlling for other comorbid psychiatric diagnoses, ADHD and ODD were more likely to co-occur in girls. One study reported the rates of comorbidity expressed as odds ratios to be 6.6 for boys and 56.3 for girls (1). An initial ADHD diagnosis is a significant predictor for later development of ODD, even after controlling for simultaneous comorbidity between the two disorders (1, 3). However, this predictive value seems largely specific to girls, possibly indicating a stronger developmental link. Physicians should therefore maintain a higher level of clinical suspicion for comorbid ODD when evaluating girls with ADHD (6). Additionally, both a latent class analysis study and a retrospective chart review found ODD to be more common with the combined subtype rather than with the inattentive subtype of ADHD (7). This finding may reflect, or even partially account for, the greater functional impairment that occurs secondary to the impulsivity observed in children with the combined type.

Screening for ADHD and ODD

The similarities between presenting symptoms that fulfill both ADHD and ODD criteria can result in challenges for accurate diagnosis of the two disorders, especially when individuals exhibit traits of both. Clinical assessment of risk factors and specific behaviors is therefore essential when evaluating comorbid ODD in children presenting with ADHD. Specific screening tools may also prove valuable in identifying comorbidities in children with ADHD, although at present few have been validated for diagnosis of ODD. One study found that the Vanderbilt ADHD Diagnostic Parent Rating Scale comorbidity screening subscales may be clinically useful in ruling out a diagnosis of ODD in children between ages 7 and 11 with underlying ADHD (8). This measure consists of questions based on a specific group of behaviors related to DSM-IV criteria for ODD and allows clinicians to compare children's scores with those from previously defined cut-off thresholds for diagnosis.

TABLE 1. DSM-IV Criteria for Diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD)

ADHD[a]	**ODD**[b]
Inattentive	
Careless mistakes	Frequent loss of temper
Difficulty sustaining attention	Arguments with adults
Difficulty listening	Defying adults' rules
Does not follow instructions	Deliberately annoying people
Lack of organizational skills	Easily annoyed
Reluctance to engage in tasks that require sustained effort	Anger and resentment
Loses things easily	Spitefulness
Forgetful	Blaming others for mistakes or misbehavior
Easily distracted	
Hyperactive-impulsive	
Restlessness	
Difficulty engaging in quiet activities	
Driven by a motor	
Excessive talking	
Blurts out answers	
Difficulty waiting turn	
Often interrupts	

[a] A diagnosis of ADHD requires at least 6 months of maladaptive symptoms, with at least six symptoms of either inattention or hyperactivity or both for combined type. Onset must be prior to 7 years of age.
[b] A diagnosis of ODD requires 6 months of hostile/defiant behavior, with at least four of the behaviors listed.

Additionally, a review by Hamilton and Armando (9) recommends the following three screening questions for evaluating ODD in children: 1) "Has your child in the past 3 months been spiteful or vindictive or blamed others for his or her own mistakes?" (Any "yes" is a positive response.) 2) "How often is your child touchy or easily annoyed, and how often has your child lost his or her temper, argued with adults, or defied or refused adults' requests?" (Two or more times weekly is a positive response.) 3) "How often has your child been angry and resentful or deliberately annoying to others?" (Four or more times weekly is a positive response.) Three positive responses are 91% specific for meeting full criteria for ODD, whereas any negative response is 94% sensitive for ruling out ODD (9).

Effect of Comorbid ADHD and ODD

Several studies have highlighted the increasing behavioral, psychological, and familial difficulties of ADHD and ODD versus ADHD alone. Generally, these disorders together tend to present earlier and portend a worse prognosis (4). Specifically, it is believed that ADHD when ODD is present raises the likelihood of a child developing conduct disorder (10). Furthermore, ADHD is predictive of repetitive conduct problems (11). In one study specifically comparing ADHD alone with ADHD comorbid with ODD, ADHD plus ODD was associated with more severe ADHD symptoms and increased aggression and delinquency (12). Furthermore, one study demonstrated that overt criminal activity is increased in juveniles with dual diagnoses versus ADHD or ODD alone. In first-time offenders, combined ADHD and ODD/conduct disorder was associated with increased likelihood of persistent high-level criminal offenses (13).

Interpersonal relationships within the family environment can also be affected by traits of ODD in individuals diagnosed with ADHD. In an attempt to evaluate the effect of interpersonal relations, one study did not specifically examine children with both diagnoses but rather assessed the effect of externalizing comorbidities (including argumentativeness, rule breaking, and symptoms of ODD) on sibling relationships. The authors found that children with ADHD and externalizing comorbidities scored lower on ratings of conflict and warmth/closeness when assessed by their siblings and that the externalizing problems (i.e., ODD symptoms) were the main predictor of those outcomes (14). Research has also assessed global social problems, including those outside family environments. Results determined that compared with conduct disorder, ODD and ADHD separately were more predictive of poor social function and anxiety (15). Additional studies have demonstrated that patients with comorbid ADHD and ODD exhibit impaired working and long-term memory, with implications on both storage and executive function, in excess of the deficits observed in patients diagnosed with a single disorder (16). These studies highlight the importance of timely diagnosis and symptom management for children with comorbid diagnoses in order to prevent potentially irreversible impairments in social and cognitive functions.

Comorbid ODD also predisposes individuals to a number of further psychiatric diagnoses in adulthood. One study found that patients with dual diagnoses had a higher lifetime risk of developing bipolar disorder, anxiety disorders, and substance abuse disorders (17). Additionally, patients with dual diagnoses who developed other psychiatric disorders did so at a younger age for every category of disorder studied except bipolar disorder. This increased likelihood of serious psychiatric comorbidities underscores the need for early screening and vigilance regarding new-onset psychiatric symptoms in patients with ADHD and ODD.

Treatment

Despite the gravity of ADHD/ODD comorbidity, evidence regarding responsiveness of ODD symptoms to ADHD treatments is generally positive. A 2002

meta-analysis of 28 studies demonstrated that stimulant medications significantly reduce symptoms of overt aggression based on clinician, parent, and teacher rating scales (18). Generally, methylphenidate was found to improve oppositional symptoms, whereas studies regarding the efficacy of atomoxetine and clonidine for oppositional symptoms revealed mixed results. Behavioral therapy indicated in the treatment of ADHD and ODD separately appears to be effective when treating the disorders together (4).

Conclusions

Although comorbid ADHD and ODD can present unique challenges to the physician and parent, there is increasing evidence from psychiatric research to guide clinical decision making. Primarily, the physician must consider demographic and other risk factors in assessing and ultimately screening children for both disorders. Once a diagnosis of ADHD and comorbid ODD is established, it is helpful to explain the unique difficulties posed by comorbidity to all involved while emphasizing the helpful role of both pharmacology and behavioral therapy in treating symptoms of both disorders.

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Working Memory Deficits in ADHD

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Attention deficit hyperactivity disorder (ADHD) is associated with working memory deficits that are amenable to treatment. ADHD is characterized by inattention, hyperactivity, and impulsivity. Approximately 5% of children worldwide have ADHD (1).

The disorder is found in community samples in a 3:1 male-to-female ratio, but a 9:1 ratio has been reported in clinical samples (2). Clinically, ADHD often presents with other disorders. Examples of comorbid conditions include oppositional defiant disorder, conduct disorder, pervasive developmental disorder, bipolar disorder, anxiety disorders, sleep disorders, Tourette's syndrome, fragile X, lead poisoning, central auditory processing disorder, and hearing problems.

Working Memory

Working memory is the ability to maintain information for a period of time before acquiring additional information in order to act upon the previously saved information. Results from a meta-analysis (3) as well as from various studies (4) are highly consistent in that working memory has been found to be impaired in children with ADHD relative to children without ADHD. Working memory is an important component of executive function, which is involved in a child's ability to formulate plans of action, test hypotheses, benefit from feedback, and work toward an end goal (5). Childhood memory impairment can also have a negative effect on the development of language, social skills, and interpersonal relationships, as well as on secondary consequences such as low self-esteem (6).

The most widely accepted model of working memory was proposed by Baddeley and Hitch in 1994 (7). This model involves a central executive (an attention control system responsible for manipulating information), a phonological loop (for maintaining and rehearsing verbal information), and a visuospatial sketchpad (for storing visuospatial information). The phonological loop plays a crucial role in learning new verbal memory associated with language acquisition, including vocabulary and word decoding (8). Impairments on measures of central executive function and in visuospatial memory are closely associated with poor academic performance in literacy, comprehension, and arithmetic (9). Children with poor working memory are slow to learn in the areas of language, reading, or mathematics, particularly on central executive and visuospatial tasks, compromising academic achievement (9). A poor reader is more likely to avoid reading, and thus the problem is never addressed. In the Connecticut Longitudinal Study, 70% of children with reading disabilities in the third grade still struggled with reading in grade 12 (10). (For examples of working memory and other types of memory, see Table 1.)

Assessing Working Memory

To provide the most comprehensive working memory assessment, one can use either the Working Memory Index or the Wechsler Intelligence Scale for Children (11), which is based on three subtest scores: forward and backward digit recall and letter number sequencing. Specialized working memory test batteries, such as the Working Memory Test Battery for Children (12) and the Automated Working Memory Assessment (13), are useful for broader evaluation of a child's profile of working memory strengths and weaknesses. These working memory assessments are valuable prospective indicators at school entry for children at risk for poor academic progress.

Treatment of Working Memory in ADHD

Attention is critical in order for information to be processed into memory. In one study (14), the administration of methylphenidate improved cognitive attention as measured by the Test of Everyday Attention for Children. In particular, sustained attention improved the most with methylphenidate treatment. Methylphenidate is a short-acting psychostimulant, with a 1- to 4-hour duration of action and a 2- to 3-hour half-life. Its mechanism of action is increasing synaptic dopamine and noradrenaline levels by blocking their reuptake in the frontostriatal re-

TABLE 1. Types of Memory

Type	Example
Immediate memory	Remembering a phone number for a brief period of time.
Short-term or working memory	Remembering to carry over a number during subtraction.
Long-term memory	Remembering events across the lifespan.
Explicit or declarative memory	Remembering facts, such as the capital city of a country.
Implicit or procedural memory	Remembering how to drive a car.
Perception representation system	Remembering sensations via the amygdala, such as texture, sight, sound, smell, and taste.

gions of the brain. ADHD affects only two lobes: the frontal (which integrates all information) and the parietal (which processes sensory information). Dopamine is associated with motivation and reward, and its presence during seemingly mundane tasks allows interest in the task to be maintained and performance to be improved. Attention difficulties increase with task complexity, suggesting that methylphenidate assists more with elaborate academic tasks.

In particular, visuospatial memory is improved with methylphenidate as measured by the Cambridge Neuropsychological Test Automated Battery. This is consistent with findings demonstrating that methylphenidate affects right hemispheric structures to a greater extent than left-sided structures (15). However, in patients with comorbid anxiety, methylphenidate does not improve working memory, since worrying is verbally mediated and consequently interferes with auditory-verbal working memory but not visuospatial working memory. Furthermore, anxious arousal is linked with the right prefrontal cortex, which may compete and interfere with cognitive operations of the right prefrontal cortex (16). Studies of verbal working memory are not as conclusive. Simple span tasks (forward tasks for storage and backward tasks for executive functions) have shown that methylphenidate is of no benefit, whereas different studies involving a more complex methodology (such as N-back tasks) have shown that methylphenidate does indeed improve verbal memory.

Nonstimulant medications can also be useful in improving working memory. Tasks of spatial working memory can be modulated by α_2-noradrenergic receptor agonists. Atomoxetine has been shown to improve spatial working memory (17). Atomoxetine is a selective noradrenaline reuptake inhibitor that inhibits the presynaptic norepinephrine transporter. It augments norepinephrine levels and indirectly increases dopamine in the prefrontal cortex without increased catecholamine in the nucleus accumbens, and thus it lacks the addictive properties of stimulants. In addition, atomoxetine does not interfere with sleep or exacerbate tics. However, effects of atomoxetine on working memory do not significantly emerge until the 12th week of treatment (17).

Nonpharmacological studies have suggested that motivational incentives improve manipulation of information but not storage, as incentives prevent a decrement in remembering previously stored information. Continuous reinforcement enhances visuospatial working memory in ADHD. In children with ADHD, removal of incentives may be a more powerful stimulus than the addition of incentives. In fact, computer working memory exercises over 5–6 weeks improved working memory in 7- to 12-year-old boys with ADHD (18). Dawson and Guare (19) suggested that children with working memory weakness may benefit from external support systems (e.g., visual cues, checklists, coaching) to help them remember specific goals and procedures.

Future Goals

Future directions include longer follow-up studies and examining the various subtypes of ADHD. Limitations for future directions of treatment targeting working memory include lack of a meaningful control group during follow-up evaluation, parents and teachers not being blind to the study, and the issue of ecological validity in determining whether results carry over outside of the laboratory (20).

Conclusions

It is vital to help children with ADHD more easily encode, access, and retrieve information by providing treatment and support for working memory limitations that reduce functional impairment. Children's academic progress during the early years of school is closely linked with working memory skills. Valuable screening methods to assess working memory should be offered to children who are at risk for poor scholastic progress. Children with ADHD later become at risk for a myriad of problems related to academic difficulties, which result in their reduced self-esteem and possibly giving up on themselves, and this may lead to a downward spiral resulting in peer selection that influences them in a negative way and substance abuse, as well as unemployment and poverty in adulthood.

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Off-Label Pharmacologic Treatments for Attention Deficit Hyperactivity Disorder: A Review

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Attention deficit hyperactivity disorder (ADHD) is a common neurobehavioral disorder in children and adolescents that often persists into adulthood. ADHD is characterized by unacceptable levels of inattention, impulsivity, and hyperactivity. Children with ADHD are at higher risk for developing comorbid mood, conduct, and substance use disorders (1). The Food and Drug Administration (FDA) has approved both stimulant and nonstimulant medications for treatment of ADHD. Stimulants are considered to be first-line treatment. However, between 10% and 30% of children do not respond to stimulants or are unable to tolerate associated side effects. For children and adolescents who do not benefit from or cannot tolerate these medications, there are other options that have not been approved by the FDA but have shown to be efficacious and tolerable. The present article focuses on the efficacy and tolerability of bupropion, desipramine, and modafinil for ADHD treatment.

Bupropion

The FDA indications for bupropion include treatment of adult depression and smoking cessation, but it is not officially approved for treatment of any child or adolescent condition. However, bupropion has clinically been used as an off-label treatment for ADHD in the juvenile population and may provide benefit in comorbid conditions such as depression, which can occur up to four times as often in ADHD youths compared with the general adolescent population (2). The mechanism of action on ADHD symptoms is thought to be through noradrenergic agonist activity and, to a lesser extent, dopaminergic agonist activity.

In a randomized, double-blind crossover study, Barrickman et al. (3) compared bupropion immediate release with methylphenidate in 15 youths (ages 7–17 years old) and found a response rate that was equivalent based on improved scores on the Iowa Conners' Teacher Rating Scale. In another randomized, double-blind placebo-controlled study, Conners et al. (4) examined 109 children (ages 6–12 years old) and reported improvements with bupropion immediate release based on scores on both parent and teacher rating scales, although the effect size was small and the improvement was less pronounced in the parent rating scale. A randomized, open-label single-blind placebo lead-in study examined adolescents (ages 11–16 years old) with ADHD and comorbid major depressive disorder or dysthymia and found that bupropion sustained release improved both ADHD and depressive symptoms in 14 (58%) of 24 children, while seven (29%) children showed improvement in depressive symptoms only, and one (4%) child exhibited improvement in ADHD symptoms only (5).

Bupropion has shown to be relatively well tolerated in children and adults. Reported side effects include rashes, irritability, tremors, and tics (5). Studies of bupropion immediate release have indicated an increased seizure risk in adults, of up to 4 in 1,000, especially in individuals with a history of seizures or eating disorders. The sustained- and extended-release formulations are thought to produce lower seizure risks due to their lower peak plasma levels. In a surveillance study of bupropion sustained release, the seizure risk in adults was found to be one in 1,000, which is a quarter of the risk seen with the immediate-release formulation (6).

Desipramine

The FDA indications for desipramine include treatment of depression in adults, but it has no official indications for children or adolescents. Desipramine is a tricyclic antidepressant that is thought to have beneficial effects for ADHD by selectively blocking norepinephrine reuptake at the presynaptic transporter. It may be particularly beneficial in children and adolescents who suffer from a comorbid tic disorder, including Tourette's syndrome. Drug levels of this medication can be monitored, although there is no established therapeutic range (7).

One randomized, double-blind placebo-controlled study included 41 participants (ages 5–17 years old) who carried a DSM-IV diagnosis of ADHD combined type and chronic motor tic disorder, chronic vocal tic disorder, or Tourette's syndrome. The ADHD symptom response rate in the treatment group was 71%, compared with 0% for the placebo group. Desipramine also significantly reduced tic symptoms, with a 58% response rate, compared with a 5% response rate for placebo (8). In another randomized, double-blind placebo-controlled study, desipramine was compared with placebo in 62 clinically referred children and adolescents, 43 of whom had previously responded poorly to treatment with stimulants. A clinically and statistically significant difference in response rate was found, with 68% of participants in the desipramine group showing good improvement, compared with only 10% in the placebo group (9).

Adverse effects of desipramine include dry mouth, blurred vision, constipation, decreased appetite, sweating, tachycardia, increased blood pressure, ECG changes, orthostatic hypotension, drowsiness, insomnia, and mood instability (7). In terms of cardiovascular parameters, desipramine has been shown to increase diastolic blood pressure and pulse rate (8). Dose-dependent changes in conduc-

tion parameters on ECGs have also been reported, including increased incidence of intraventricular conduction defect of the right bundle branch type (10). There have been four sudden deaths reported in children taking desipramine, and although a causal link has not been established in these cases, there has been concern about QT prolongation as a possible mechanism (11).

Modafinil

The FDA indications for modafinil are reserved for treatment of excessive sleepiness in narcolepsy, shift work sleep disorder, and obstructive sleep apnea. Nevertheless, it is a medication that is used as an off-label treatment for ADHD. Compared with stimulants, it has a different mechanism of action, novel therapeutic uses, and less abuse potential. Its method of action is thought to be due to its modulation of the release of glutamate, gamma aminobutyric acid, histamine, and hypocretin. Conventional stimulants cause diffuse neuronal activation, while modafinil results in hypothalamus-based wakefulness.

In a pooled analysis of three randomized, double-blind placebo-controlled studies, modafinil, compared with placebo, demonstrated improved efficacy and significant improvement in symptoms based on the ADHD Rating Scale-IV, School and Home versions, with a collective effect size of 0.69 (12). This analysis also revealed that modafinil treatment resulted in improved symptoms in children and adolescents who had received stimulant treatment in the past. In a separate randomized double-blind study comparing a single use of modafinil with methylphenidate administered several times over a 2-week period, 17 of 28 (61%) participants exhibited improvement with modafinil, based on the Test of Variables of Attentions, compared with 16 of 28 (58%) participants who received methylphenidate (13). These results were not significantly different and highlight the efficacy of modafinil when compared with stimulants.

Modafinil has been fairly well tolerated in children and adolescents. Side effects include appetite suppression, insomnia, and headache (12). Importantly, in various studies, discontinuation due to side effects has been shown to not be significantly different between modafinil and both placebo and methylphenidate (14). In fact, modafinil's tolerable side-effect profile has been considered one of its potential advantages in the treatment of ADHD (15). The FDA has not approved modafinil because of its minor risk of causing Stevens-Johnson syndrome (16). Interestingly, several cases of serious or suspected skin reactions as likely related to modafinil have been reported among nearly 1,000 children and adolescents; just five similar cases have occurred worldwide in 680,000 adults who received modafinil for other reasons.

Conclusions

Bupropion, desipramine, and modafinil have all shown evidence of efficacy in the treatment of ADHD in children and adolescents. Bupropion appears to provide added benefit in the presence of comorbid major depression or dysthymia, and it may be a reasonable choice if there are relative contraindications to stimulant use, such as concerns about substance abuse, cardiac abnormalities, or poor tolerability. Desipramine has been shown to be beneficial in children and adolescents with comorbid tic disorders, but its use in this population is no longer favorable because of the sudden and unexplained deaths of four children taking the medication. Other TCAs, such as imipramine and nortriptyline, are often used as alternative agents, but data supporting their use are not as robust (11). Modafinil's benefits include fewer reported adverse effects and less dependency potential than methylphenidate and other stimulants. There needs to be more large-scale studies measuring the effectiveness of modafinil; however, it has been shown to be an acceptable choice of treatment when children and adolescents do not respond to methylphenidate or other stimulants.

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Correlation and Treatment of ADHD in Substance Use Disorders

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Attention deficit hyperactivity disorder (ADHD) is a highly prevalent psychiatric disorder with core symptoms of impulsivity, inattention, and hyperactivity. A body of evidence suggests that there is increased prevalence and severity of substance use disorders among individuals meeting diagnostic criteria for ADHD. The economic costs of substance use disorders are estimated to be about $600 billion annually for both health- and punitive-related expenses (1). Among individuals with substance use disorders, those who meet criteria for comorbid ADHD have an earlier age at onset of dependence and greater risk of suicide attempts, and they use a greater number of substances (2). The prevalence of ADHD in people with substance use disorders is estimated to be 23%, according to a major meta-analysis reporting data on 6,689 subjects (3). This significant correlation is seen irrespective of demographic factors, including gender, age, and ethnicity.

Several theories have been proposed to explain the relationship between ADHD and substance use disorders. Functional MRI studies have shown that dopamingeric activity in the caudate and areas of the limbic system is depressed in individuals with ADHD. This dopaminergic dysfunction is thought to be related to coexisting substance use disorders, since many substances that are abused stimulate a surge or release of dopamine (4). Genetically predisposed traits, such as novelty seeking and impulsivity, are common between the two conditions, and this may be a result of shared neurobiological mechanisms. In a study of 18 multigenerational families from a genetically isolated area with a high prevalence of ADHD, linkage analysis implicated a variant of the *LPHN3* gene. The product of this gene, latrophilin 3, is a G protein-coupled receptor that has been recognized to have a prominent role in neuronal transmission and maintenance of neuron viability (5). This variant is expressed in areas of the brain related to attention and activity (the amygdala, cerebellum, and caudate nucleus). This gene has also been implicated in the locus of key variants in individuals with alcohol abuse problems and individuals who use illegal substances (6). Furthermore, this same genetic locus has been associated with positive therapeutic response to stimulant medication at both the marker ($p<0.05$) and haplotype ($p<0.01$) level (7).

Diagnostic challenges await clinicians working with patients with substance use disorders because there is a degree of symptom overlap with ADHD. Impulsiveness, impairment in concentration, and extreme restlessness may present in both diagnoses (8). At present, no formal validated scales exist to aid in the diagnosis of ADHD in patients with substance use disorders. One recent study used the Adult ADHD Self-Report Scale in the assessment of 183 patients with substance use disorders. Findings revealed that there was a higher false positive rate for patients than for the general public (9).

Stimulant-based medication remains the first-line treatment for ADHD. However, controversy exists regarding the prescribing of stimulant medications for patients with current or prior substance use disorders. It has also been proposed by some that the stimulants used to treat ADHD may increase the risk of developing a substance use disorder. McCabe et al. (10) conducted a web survey of 9,161 college students and found the reported misuse of stimulants to be 8.1% (10). However, there are data to support that pharmacotherapy treatment for ADHD aids in maintaining abstinence in patients with substance use disorders. One study reported a decrease in cocaine use when patients were treated with methylphenidate. Measured by the number of cocaine-positive urine samples, methylphenidate, compared with placebo, significantly decreased use ($p=0.001$). The study also found that methylphenidate improved ADHD symptoms in cocaine users (11).

When early intervention is initiated, it may prevent the development of subsequent substance use disorders. Biederman et al. (12) found that untreated ADHD was a significant risk factor for substance use disorders in adolescence, whereas children receiving pharmacotherapy had an 85% reduction in risk (12). To aid in treatment, nonstimulant pharmacological treatments are also available. Atomoxetine is a selective-noradrenergic reuptake inhibitor with low abuse potential. Decreased ADHD symptoms have been observed in patients with comorbid ADHD and alcohol abuse when treated with atomoxetine. However, while ADHD symptoms may improve, the effect on alcohol use is minimal (13). Antidepressants, such as desipramine, bupropion, and monoamine oxidase inhibitors (pargyline and selegiline), all of which have low abuse potential, have also been used to treat ADHD. However, the use of monoamine oxidase inhibitors has only showed modest effects. Use of the tricyclic antidepressant desipramine has shown significant improvement in symptoms when administered in adults at a dose of 200 mg daily. (14) In one study of patients with both substance use disorders and ADHD, bupropion was successfully used to treat ADHD, with a significant reduction in symptoms as measured on the ADHD Rating Scale and the Clinical Global Impres-

sions-ADHD severity (15). However, no improvement in the subjective use of substances was reported. Work in developing new, abuse-resistant medications has begun. Lisdexamfetamine, a newer Food and Drug Administration-approved drug treatment, is thought to have lower abuse potential. This is believed to come from its rate-limiting enzymatic cleavage to an amino acid and active agent, D-amphetamine, which extends the duration of effect and limits abuse (16).

In conclusion, there appears to be a high correlation between ADHD and substance use disorders. Challenges for diagnosis exist given the possible overlap of symptoms. In remaining aware that ADHD patients are at increased risk for developing substance use disorders, physicians can be proactive in both preventing and quickly treating emerging substance use disorders. Initiating treatment regimens early in the course of ADHD, as well as prescribing long-acting stimulants, may help decrease comorbid substance abuse. Treatment options exist, and there are differing levels of efficacy with use of nonstimulant medications. More research in this field is required to develop diagnostic tools, as well as treatment strategies, for patients with or at high risk for substance use disorders.

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Case Report

Dyskinesia Induced by Mixed Amphetamine Salts

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Stimulant medications are approved for treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy. Cardiovascular adverse events, gastrointestinal upset, anorexia, and insomnia are common side effects of this drug group. Orofacial or limb dyskinesia has infrequently been documented (1–3). Other movement disorders that can result from the use of this psychopharmacological group include chorea and nocturnal bruxism (4–5). We present a case of dyskinesia that developed in a child with ADHD after initiation of mixed amphetamine salts.

Case

"Joseph" was a 6-year-old Latino child who had been treated for ADHD combined type and phonological disorder. He was hyper, had decreased concentration, and was easily distracted, which were symptoms reported since age 4. Although his motor development was normal, a significant speech delay was prominent, necessitating speech therapy since age 2. Recurrent ear infection, which was treated with bilateral tympanostomy tube placement, was the only medical issue. The patient had no history of antipsychotic drug treatment and no personal or family history of tics or other movement disorders. In November 2010, methylyphenidate extended release was initiated at a dose of 18 mg daily and continued for 1 year. Four months before discontinuation, the dose was increased from 27 mg to 36 mg daily. Although the patient's hyperactivity, impulsivity, and inattention improved, the medication was discontinued due to stomach upset, and mixed amphetamine salts extended release (15 mg daily) was initiated. During the two subsequent monthly visits, the treatment was maintained due to symptom improvement and stable vital signs (blood pressure=80/60; weight=20.75 kg; height=112 cm; body mass index=16.5 kg/m^2). Emotionality and excessive crying were the only negative events reported. During the third month of treatment, the child's mother expressed concern about persistent, fast, and repetitive lateral jaw movement. This dyskinesia persisted, without other associated facial or limb movements, even when the child was distracted. The dyskinesia symptoms disappeared with no residual effects within days following a dose decrease to 5 mg daily. The child had no major behavioral or attention problems in school or at home thereafter, although he was lost to follow-up after 2 months of low-dose amphetamine treatment.

Discussion

Orofacial or limb dyskinesias are a rare consequence of stimulant use. Review of the literature suggests that symptom onset ranges between 30 minutes and 23 months after stimulant medication initiation. The rapid developing type may be secondary to high serum drug levels, leading to dopamine receptor overstimulation (1, 2). The slower occurring type may signify dopamine receptor upregulation/hypersensitivity (1). Complete dyskinesia resolution in the published cases occurred 5 hours to 4 weeks postmedication discontinuation. Risk factors in pediatric populations include long-term stimulant use, higher dosage increments, and preexisting basal ganglia dysfunction, as well as when the medication is combined with a neuroleptic agent (5).

Methylphenidate extended release 36 mg is thought to be equivalent to 15 mg of mixed amphetamine salts extended-release and was within the expected therapeutic range in the above case. Yet, differences in formulations and rates of ingredient release may explain higher than desired drug blood levels, with the latter drug leading to emotional lability or dyskinesia. Controversy exists concerning continuation of the offending medication and the outcome of these side effects; risk with continuing the medication, precluding trying the alternative, outweighs the benefit. Medication dose decrease or discontinuation leads to complete disappearance of movement disorder side effects, as reported in all published cases. Contrary to our case, the methylphenidate formulation was the causative agent in most case studies, with only one case correlated to dextroamphetamine.

The present case emphasizes the importance of caution when changing from one form of stimulant medication to another. Monitoring for movement disorders, using the Abnormal Involuntary Movement Scale, in the first few months of medication initiation or increase might be essential to early detection of adverse events.

Dr. Sedky is a second-year child and adolescent psychiatry resident in the Department of Psychiatry, Drexel University School of Medicine, Philadelphia.

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2. Heinrich TW: A case report of methylphenidate-induced dyskinesia. Prim Care Companion J Clin Psychiatry 2002; 4: 158–159
3. Balazs J, Besnyo M, Gadoros J: Methylphenidate-induced orofacial and extremity dyskinesia. J Child Adol Psychopharmcol 2007; 17:378–381
4. Mendhekar DN, Andrade C: Bruxism arising during monotherapy with methylphenidate. J Child Adolesc Psychopharmacol 2008; 18:537–538
5. Morgan JC, Winter C, Wooten GF: Amphetamine-induced chorea in attention deficit-hyperactivity disorder. Mov Disord 2004; 19:840–842

Book Review

Delivered from Distraction: Getting the Most Out of Life with Attention Deficit Disorder

Justine Wittenauer, M.D.
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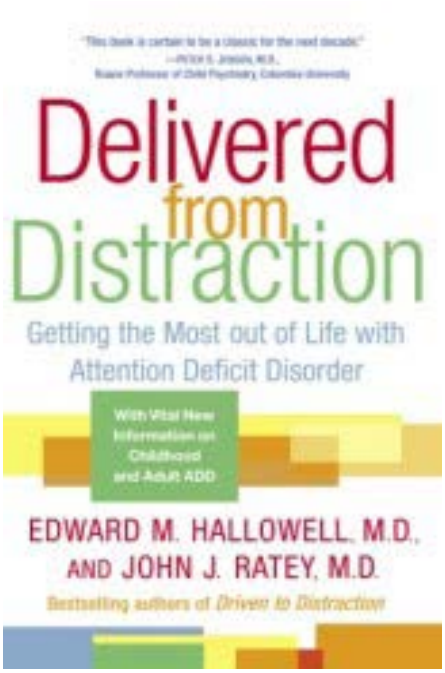
Delivered from Distraction: *Getting the Most Out of Life With Attention Deficit Disorder* is a guide for individuals who are affected by attention deficit hyperactivity disorder (ADHD). The target audience includes families, patients, and clinicians, as well as anyone who may be curious about what it means to have ADHD. Written by the notable authors of *Driven To Distraction: Recognizing and Coping with Attention Deficit Disorder from Childhood Through Adulthood* (1), the book details living and coping strategies for those who have ADHD. Goals include the provision of information about the diagnosis of ADHD, elaboration on different treatment strategies, and creation of a positive outlook on a disorder that is often viewed as an affliction. Older, traditional treatment options are discussed, while newer, less explored therapies are outlined as possibilities for the future.

Divided into four main sections, the book begins with an amusing chapter titled "The Skinny on Attention Deficit Disorder: Read This If You Can't Read the Whole Book." Throughout the book, the authors' sense of humor emerges, as demonstrated in the chapter on attention deficit disorder self-assessment, where an item is deliberately omitted, and test takers are later reminded of the item and told that they probably forgot the omission due to distractibility. This sense of informality, which makes the book one of mass appeal, may turn away some professionals. Throughout the book, the term attention deficit disorder rather than ADHD is used because it is more commonly recognized by lay individuals. As clinicians, it may be difficult for us to understand the use of a nonstandard medical term. Whether by coincidence or by design, hyperactivity is minimally addressed.



Delivered from Distraction: Getting the Most Out of Life with Attention Deficit Disorder

by Edward M. Hallowell, M.D., and John J. Ratey, M.D. New York, Ballantine Books, 2005, 380 pp., $16.00.

Subsequent sections describe individuals with attention deficit disorder, challenges their families experience, clinical diagnoses, and treatment methodologies. The section titled "Making the Diagnosis of Attention Deficit Disorder" is one of the more interesting and controversial parts of the book in that it encourages readers to seek diagnosis and treatment through almost everyone except general adult psychiatrists because they are "notoriously weak in this area." While this may or may not be true, it was surprising that family physicians, child psychologists, and general pediatricians would be ranked higher than general adult psychiatrists with regard to making this diagnosis in adults.

Although some controversial opinions, such as use of the outdated term attention deficit disorder, are presented, this book is both engaging and informative. It is easy to navigate and keeps the reader's attention via frequent use of illustrative examples. Part of the book's appeal is that it provides valuable life-coping mechanisms for those with ADHD. This treatise is a much needed quality book for patients and families. It is also a must read for mental health professionals. The book not only assists in abandoning possible preconceived notions but also acts as a guide to maximize human potential in both children and adults.

Dr. Wittenauer is a third-year resident in the Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta.

Reference

1. Hallowell EM, Ratey JJ: Driven To Distraction: Recognizing and Coping with Attention Deficit Disorder from Childhood Through Adulthood. New York: Pantheon Books, 1994

Letter to the Editor

To The Editor: In their article titled "A Direct Comparison of Lecture and E-Mail Subgroups of a National Board of Medical Examiners Psychiatry Subject Examination Review Session," published in the May 2012 issue, Shawn Sidhu, M.D., et al. (1) chose to focus on a critically important topic. There is certainly an enormous amount of material that must be learned during a physician's medical education. Improving the process to make learning more efficient regarding time spent and more effective regarding material retained is of significant benefit to medical professionals. Unfortunately, the Sidhu et al. study has several limitations, primarily as a result of the methodological design.

A key element in any scientific experiment is reproducibility. The method used in this study would make reproduction difficult for an outside observer to accomplish. The process used in creating questions for the review material was somewhat unclear. It would have been helpful if a copy of the document given to medical students had been included in an appendix to further elucidate this process.

How the resident leader was prepared for the role of leading small groups and how learning in the small groups was accomplished appear to be critical to the problem-based learning approach. However, these elements were not thoroughly addressed. A more detailed explanation of these points is warranted.

The data and data analysis are difficult to decipher. Presenting the results visually with a chart or graph would help readers better understand the findings. In addition, little numerical information is provided. The article includes mean raw scores and p values. Inclusion of values for median, mode, standard deviation, range, low score, high score, and 95% confidence interval would have made for a much stronger presentation. Furthermore, the defined subgroups mentioned in the methods section were not addressed in the results section. It would be interesting to learn whether the efficacy of the approach remained the same throughout the year.

Most importantly, the authors cannot support the conclusion that the scores in the lecture and e-mail subgroups were improved relative to scores in the comparison group as a result of the intervention. A covariate analysis is mentioned; however, there is a lack of accompanying data to verify the results. Without this information, the actual difference between the groups is unknown. While it is possible that the problem-based learning approach is the reason for the reported difference, there are alternate explanations. For example, one class of students may have simply been better academically than the other. Another possible explanation is that the psychiatry professor could have been a different person from one academic year to the next. If the professor remained the same, then his or her teaching effectiveness could have improved between the two academic-year classes. Ultimately, it is unclear what potential variables could have contributed to the reported difference in test scores. A better approach might have been to compare two intervention groups using random assignment with a comparison group in the same academic-year class.

Maximizing learning effectiveness is a laudable goal for medicine or any other profession, and Sidhu et al. should be applauded for their work in examining this process. However, they cannot conclude based on the data provided in their article that problem-based learning is more effective than other methods.

Reference

1. Sidhu S, Chandra RM: A direct comparison of lecture and e-mail subgroups of a National Board of Medical Examiners Psychiatry Subject Examination review session. J Am Psychiatry Res Journal 2012; 7(5):11–12

Stephen Welch, M.D.
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Response to Welch Letter

To the editor: We agree with Dr. Welch in that our intervention could be described in more detail. In general, specific elements of novel curricular interventions, treatment manuals, and symptom scales are often not revealed in journal articles because of intellectual property concerns.

Concerning how the resident leader was prepared to teach, there was little to no preparation in this regard, since the review consisted of short-answer questions in which students took turns answering. Questions the students could not answer or could only partially answer were filled in by the first author of our study. In retrospect, perhaps our use of the term "problem-based learning" was problematic, or at least unclear. The document was a fill-in-the-blank review sheet covering key areas of the National Board of Medical Examiners shelf examination, and students answered questions aloud, with the first author correcting them or supplying unknown answers.

The critiques of our study design and limited data are generally valid. However, since this was a secondary analysis of the effectiveness of the review session as a whole, we limited the data. Covariate analysis via analysis of variance calculations using command-prompt software programs is a widely accepted statistical method used to eliminate potential confounding factors. Therefore, we felt that it was sufficient to rule out differences between academic-year classes. At the same time, factoring in average or individual United States Medical Licensing Examination step I scores for the classes might have added more credibility to this portion of our findings. While the gold standard of trials is the randomized, controlled trial and the equivalent would have been to compare groups within the same class, the educational institutional review board would not have approved a study that gave a potentially useful intervention to two groups of students but not to a third. In addition, the students might have been dissatisfied with the nonlevel playing field, given that clerkship grades influence residency placement.

We appreciate the process of being able to view and respond to constructive criticism regarding our article.

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Semela Neuropsychiatric Institute, Los Angeles
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Massachusetts General Hospital, Boston

CALL FOR PAPERS

Have You Ordered a Lab Today?

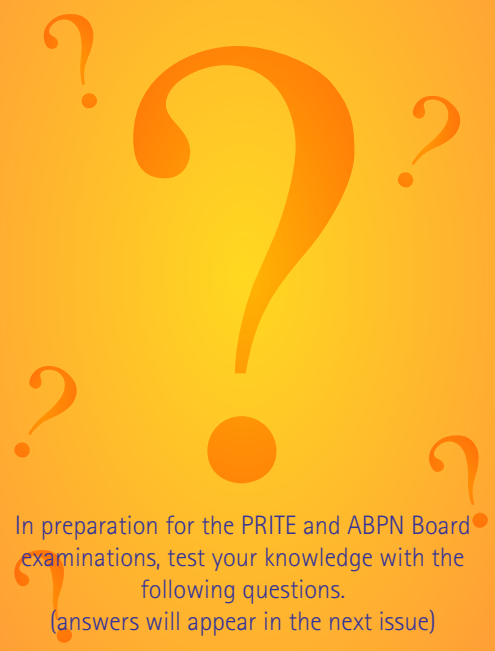
The Residents' Journal is soliciting manuscripts about the use of laboratory studies in clinical care.

Suggested topics are:

- The measurement of serum antipsychotic levels
- The role of laboratory studies in managing substance use disorders
- Laboratory studies for specific populations (e.g., children, pregnant women)
- The laboratory monitoring of clozapine's systemic effects

Please note that we will consider manuscripts outside of the suggested topics.

TEST YOUR KNOWLEDGE



In preparation for the PRITE and ABPN Board examinations, test your knowledge with the following questions.
(answers will appear in the next issue)

In preparation for the PRITE and ABPN Board examinations, test your knowledge with the following questions (answers will appear in the next issue).

This month's questions are courtesy of Justine Wittenauer, M.D. Dr. Wittenauer is a third-year resident in the Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta.

Question #1

For children receiving stimulant treatment for attention deficit hyperactivity disorder (ADHD), discontinuation of these medications (or "drug holidays") during nonschool days, such as weekends or summer breaks, corresponds with which one of the following answers:

A. Is routinely recommended for all patients receiving stimulant medications

B. Has not been shown to significantly reduce insomnia symptoms

C. May be beneficial for those with growth retardation

D. May be used with the nonstimulant drug atomoxetine

Question #2

Atomoxetine is a nonstimulant medication used for the treatment of ADHD. Which of the following is not a contraindication for its use?

A. Atomoxetine treatment is within 14 days of monoamine oxidase inhibitor administration

B. History of pheochromocytoma

C. Glaucoma

D. Recent history of stroke or transient ischemic attack

ANSWERS TO JUNE QUESTIONS

Question #1

Answer: D. Under Social Security Disability Insurance (SSDI), the number of credits required to be insured correlates with the age at which the disability occurred.

SSDI and Supplemental Security Income (SSI) are federally run programs with similar medical requirements but different eligibility requirements. SSDI disperses money to disabled individuals depending on credits earned through prior work history, as well as total lifetime earnings. The number of credits required to be insured under SSDI depends on the age at which the disability occurred. SSI requires an individual to have under $2000 in assets.

Reference

1. Coffman TS: Back to Maslow's hierarchy: a federal disability benefits primer. Am J Psychiatry Res J 2012; 7(6):13–15

Question #2

Answer: B. Mental illness is the primary disability in approximately 27% of working-age SSDI recipients and 34% of working-age SSI recipients.

Reference

1. Coffman TS: Back to Maslow's hierarchy: a federal disability benefits primer. Am J Psychiatry Res J 2012; 7(6):13–15

We are currently seeking residents who are interested in submitting Board-style questions to appear in the Test Your Knowledge feature. Selected residents will receive acknowledgment in the issue in which their questions are featured.
Submissions should include the following:
1. Two to three Board review-style questions with four to five answer choices.
2. Answers should be complete and include detailed explanations with references from pertinent peer-reviewed journals, textbooks, or reference manuals.
***Please direct all inquiries and submissions to Dr. Vahabzadeh: arshya.vahabzadeh@emory.edu.**

Author Information for *The Residents' Journal* Submissions

The Residents' Journal accepts manuscripts authored by medical students, resident physicians, and fellows; manuscripts authored by members of faculty cannot be accepted.

1. **Commentary:** Generally includes descriptions of recent events, opinion pieces, or narratives. Limited to 500 words and five references.
2. **Treatment in Psychiatry:** This article type begins with a brief, common clinical vignette and involves a description of the evaluation and management of a clinical scenario that house officers frequently encounter. This article type should also include 2-4 multiple choice questions based on the article's content. Limited to 1,500 words, 15 references, and one figure.
3. **Clinical Case Conference:** A presentation and discussion of an unusual clinical event. Limited to 1,250 words, 10 references, and one figure.
4. **Original Research:** Reports of novel observations and research. Limited to 1,250 words, 10 references, and two figures.
5. **Review Article:** A clinically relevant review focused on educating the resident physician. Limited to 1,500 words, 20 references, and one figure.
6. **Letters to the Editor:** Limited to 250 words (including 3 references) and three authors. Comments on articles published in *The Residents' Journal* will be considered for publication if received within 1 month of publication of the original article.
7. **Book Review:** Limited to 500 words and 3 references.

Abstracts: Articles should not include an abstract.

Upcoming Issue Themes

Please note that we will consider articles outside of the theme.

September 2012
Section Theme: Open
E-mail Editor: Monifa Seawell, M.D.
mseawell@med.wayne.edu

October 2012
Section Theme: Psychosomatics
Guest Section Editor: David Hsu, M.D.
david.hsu@ucdmc.ucdavis.edu

November 2012
Section Theme: Transitions
Guest Section Editor: Nina Kraguljac, M.D.
nkraguljac@uab.edu

December 2012
Section Theme: Open
E-mail Editor: Monifa Seawell, M.D.
mseawell@med.wayne.edu