JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 26, Number 1, 2016
Mary Ann Liebert, Inc.
Pp. 19–25
DOI: 10.1089/cap.2015.0126

Impulsive Aggression as a Comorbidity of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents

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Abstract

Objective: This article examines the characteristics of impulsive aggression (IA) as a comorbidity in children and adolescents with attention-deficit/hyperactivity disorder (ADHD), focusing on its incidence, impact on ADHD outcomes, need for timely intervention, and limitations of current treatment practices.

Methods: Relevant literature was retrieved with electronic searches in PubMed and PsycINFO using the search strategy of ''ADHD OR attention deficit hyperactivity disorder'' AND ''impulsive aggression OR reactive aggression OR hostile aggression OR overt aggression'' AND ''pediatric OR childhood OR children OR pre-adolescent OR adolescent'' with separate searches using review OR clinical trial as search limits. Key articles published before the 2007 Expert Consensus Report on IA were identified using citation analysis.

Results: More than 50% of preadolescents with ADHD combined subtype reportedly display clinically significant aggression, with impulsive aggression being the predominant subtype. Impulsive aggression is strongly predictive of a highly unfavorable developmental trajectory characterized by the potential for persistent ADHD, increasing psychosocial burden, accumulating comorbidities, serious lifelong functional deficits across a broad range of domains, delinquency/criminality, and adult antisocial behavior. Impulsive aggression, which triggers peer rejection and a vicious cycle of escalating dysfunction, may be a key factor in unfavorable psychosocial outcomes attributed to ADHD. Because severe aggressive behavior does not remit in many children when treated with primary ADHD therapy (i.e., stimulants and behavioral therapy), a common practice is to add medication of a different class to specifically target aggressive behavior.

Conclusions: Impulsive aggression in children and adolescents with ADHD is a serious clinical and public health problem. Although adjunctive therapy with an aggression-targeted agent is widely recommended when aggressive behaviors do not remit with primary ADHD therapy, empirical evidence does not currently support the use of any specific agent. Randomized controlled trials are needed to identify aggression-targeted agents with favorable benefit–risk profiles.

Background

Behavior with the immediate intent to cause harm – whether to self, others, objects, or property – constitutes aggression. Although toddlers will often be physically aggressive when expressing anger, the use of physical aggression typically declines as cognitive and language abilities develop and children become more competent in regulating their emotions (Campbell et al. 2006). Aggressive behavior becomes maladaptive when it persists, occurs outside an acceptable social context, and is of an intensity, frequency, severity, and/or duration detrimental to the child's interests (Connor et al. 2006; Jensen et al. 2007). Maladaptive aggression is disproportionate to preceding events, can occur without an antecedent social cue, violates social rules, and does not terminate readily. Importantly, maladaptive aggression is an expression of central nervous system (CNS) dysfunction and may, therefore, be amenable to treatments targeting its neurobiologic substrate. Aggressive behavior in children accounts for 25% of special services in school (Hubbard et al. 2010) and is one of the most common causes of mental health referrals, accounting for up to 60% of child psychiatry referrals (Steiner et al. 2003; Connor et al. 2006).

Aggression can be categorized into two broad subtypes based on the aggressor's motivation: 1) Reactive or impulsive and 2) proactive or instrumental (Vitiello and Stoff 1997). Impulsive aggression (IA)

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Funding: Editorial assistance with manuscript preparation was funded by Supernus Pharmaceutical, Inc.

is angry, retaliatory aggression arising out of frustration, annoyance, or hostility to real or perceived provocations – stressors that youth of the same age typically experience with equanimity. Impulsive aggression is, therefore, an unplanned and immediate response reflecting out-of-control emotionality that satisfies immediate emotional pressures, albeit with negative consequences to the aggressor. In contrast, instrumental aggression is consciously planned, goal-oriented behavior with the specific intent of benefiting the aggressor. Although these are distinct subtypes of aggression, they both occur to varying degrees in aggressive children (Hubbard et al. 2010). Impulsive aggression, which is associated with a broad array of psychiatric disorders, is the most common phenotype in clinical populations, occurring in ~ 80% of aggressive children (Vitaro et al. 2002).

Within well-defined psychiatric disorders such as attention-deficit/hyperactivity disorder (ADHD), IA is a clinically distinct and common behavior. Impulsive aggression has been likened to fever or pain that generalizes across multiple medical illnesses and informs about the severity but not the specific nature of the illness (Jensen et al. 2007). Although IA appears to be more responsive to intervention than instrumental aggression, it is often refractory to treatments targeting the primary disorder (e.g., ADHD). Recognizing that clinicians lack evidence-based medication strategies for managing refractory IA, an expert consensus report recommended that randomized controlled trials be conducted with available drugs, which are currently being used off-label, as well as new drugs to specifically assess the efficacy and safety of medications as IA-targeted therapy (Jensen et al. 2007). This review will characterize IA in the specific context of ADHD, whereas other articles in this special edition will focus on IA associated with autism and bipolar disorder as primary disorders. Specifically, we will examine the incidence of IA as a comorbidity of childhood ADHD, its impact on the developmental trajectory of ADHD, the vicious cycle of dysfunction that warrants timely intervention, the limitations of primary ADHD therapy, and the need for empirical evidence to support current treatment practices of adding antipsychotics and/or mood stabilizers as adjunctive IA-targeted therapy.

Impulsive Aggression as a Comorbid Behavior in ADHD

According to the 2011 National Survey of Children's Health, parent-reported prevalence of diagnosed ADHD in children and adolescents is 6.8–10.2%, making ADHD the most common neurodevelopmental disorder in youth (Visser et al. 2010, 2014) Although aggression is not diagnostic of ADHD (Jensen et al. 2007; Connor et al. 2010a), it is often a prominent feature in the clinical presentation of ADHD and the impetus for the initial referral for mental health evaluation (King and Waschbusch 2010). A post-hoc analysis of data from the Multimodal Treatment Study of Children with ADHD (MTA) showed that 54% of study participants with ADHD combined subtype displayed clinically significant aggression at baseline (Jensen et al. 2007). Moreover, a multivariate regression analysis of impairment scores found that aggression had a much greater impact (~10% of variance) on parents' overall impairment ratings than core ADHD symptoms, which accounted for only ~2% of variance (Jensen et al. 2007). Because caregivers who feel they cannot manage a severely aggressive child or adolescent will often request medication changes (Jensen et al. 2007), severe aggression in ADHD increases the likelihood that non-ADHD drugs such as antipsychotics and/or mood stabilizers will be used adjunctively with ADHD medication, even though clinicians currently lack high quality evidence to guide treatment decisions.

Because aggression had not been widely studied in clinical samples of children and adolescents with ADHD, Connor et al. compared a referral ADHD population with community controls, using multiple scales to measure aggressive behaviors (Connor et al. 2010a). Children with ADHD were consistently more aggressive than community controls. Aggression exhibited a ''dose effect,'' in terms of a significant correlation between aggression severity and number of comorbid diagnoses, as well as ADHD symptom severity. Impulsive forms of aggression were significantly more common than instrumental forms for all ADHD children than for community controls, for the ''pure'' ADHD group (no comorbid diagnosis), and in each ADHD plus comorbidity subset. In analyses controlling for comorbidity, all ADHD subtypes (including a group with ADHD symptoms not meeting diagnostic criteria) were significantly more aggressive than community controls; scores tended to be highest for the ADHD combined subtype. Results, therefore, suggested that aggression is a generalized marker of ADHD severity.

In the abovementioned study, only patients meeting diagnostic criteria were counted as having a specific psychiatric comorbidity such as oppositional defiant disorder (ODD) or conduct disorder (CD). However, ODD/CD externalizing behaviors can be present at subthreshold levels in ADHD children. Connor et al., therefore, compared ADHD youth with non-ADHD controls in terms of emotional and behavioral symptoms often associated with ADHD (Connor et al. 2012). The ADHD cohort was divided into all children with hyperactive-impulsive ADHD symptoms (hyperactive subtype + combined subtype) and those with inattentive subtype only; the non-ADHD controls included a psychiatric referral group and a community control group. Those with ADHD symptoms displayed more severe aggression than children in the control groups. Externalizing behavior problems and aggression, which increased as ADHD symptom severity increased, appeared to be related to the hyperactivity-impulsivity ADHD domain.

Historically, the ADHD–aggression relationship has been viewed as one in which aggression and ADHD symptoms are separate but correlated dimensions of externalizing behavior (Waschbusch 2002; King and Waschbusch 2010) More recently, however, IA has also been attributed to emotional impulsivity/dysregulation, which appears to be a central feature of ADHD. Emotional impulsivity refers to deficits in the first step of emotional self-control; that is, the ability to inhibit strong emotional reactions to environmental events (Barkley 2010; Barkley and Fischer 2010; Barkley and Murphy 2010) Emotional dysregulation reflects deficits in the second step of emotional self-control; that is, deficits in the ability to self-regulate the emotional state to be more age appropriate, socially acceptable, and consistent with the individual's long-term well-being. Emotional impulsivity/dysregulation may be responsible, at least in part, for the co-occurrence of ADHD, IA, and externalizing ODD behaviors, which have also been attributed to emotional impulsivity/dysregulation. (Barkley and Fischer 2010; Barkley and Murphy 2010).

Although childhood ADHD was once viewed as a benign, self-limiting disorder in which symptoms remitted by adolescence, numerous prospective longitudinal studies have clearly established the negative impact of childhood ADHD and its reverberations into adolescence and adulthood. ''Life consequences'' of longitudinal ADHD studies have been broadly categorized as academic, antisocial behavior, driving, nonmedicinal drug use/addictive behavior, obesity, occupation, services use, self-esteem, and social function outcomes (Shaw et al. 2012), with the least desirable developmental trajectory being a progression from childhood ADHD to adult antisocial behavior (McKay and Halperin 2001).

Aggressiveness plus hyperactive-impulsive-inattentive behavior in children amplifies the risks of various psychological, academic, emotional, and social problems when compared with either behavior pattern alone (Shelton et al. 1998). Similarly, in later childhood and adolescence, aggressive-hyperactive-impulsive behavior versus hyperactivity-impulsivity alone is associated with markedly higher risk of persistent behavioral problems, CD, encounters with the justice system, deficits in academic achievement, behavioral and disciplinary problems at school, and substance experimentation/abuse (Satterfield et al. 1982; Campbell 1987; Walker et al. 1987; Fischer et al. 1990; Biederman et al. 1996; Mannuzza et al. 1998; Shelton et al. 1998). Although studies demonstrating the high risk of impairments in young aggressive, hyperactive-impulsive children did not differentiate aggression types, McKay and Halperin (2001) have argued that early-onset, pervasive, and unremitting IA in the context of impulsive thoughts, emotional lability, and impulsive behavior represents a high-risk profile for progression from childhood ADHD to adult antisocial disorders.

Impulsive Aggression in ADHD Children: The Lifetime Legacy of Peer Rejection

Optimal social outcomes depend on children being able to forge positive relationships with peers, because skills critical to effective social functioning – for example, cooperation, negotiation, and conflict resolution – are developed primarily in the context of peer interactions (Hoza 2007). Peer problems in general are predictive of an array of serious adjustment problems, including delinquency, substance abuse, dropping out of school, academic difficulties, and other psychopathology (Parker and Asher 1987; Hoza et al. 2005a) – impairments that have also been chronicled in association with ADHD. Therefore, it is important to understand peer relationships within the context of ADHD, particularly with regard to comorbid IA.

A range of social problems have been associated with inattention and hyperactivity-impulsivity in children and adolescents, including fewer friendships, bullying, victimization, and poor relationships with peers (Wheeler and Carlson 1994; Hoza 2007; Nijmeijer et al. 2008). Peer rejection is a common occurrence for ADHD children, with IA having an especially potent effect. At the baseline assessment for the MTA study (MTA Cooperative Group 1999), 52% of children meeting diagnostic criteria for ADHD were rejected by peers compared with 14% of their randomly selected classmates (Hoza et al. 2005b). In addition, children in the MTA study were less well liked and had fewer friends than their classmates; 56% did not have reciprocal friends, versus 32% of their classmates (Mrug et al. 2012). They were disliked by children with higher status in the peer group and, therefore, subject to being excluded by more popular peers. Moreover, deficits in peer relationships were consistent across age and gender and were well established by at least 7 years of age (lowest age at study entry).

With their noncompliant, disruptive, and aggressive behavior, ADHD children are almost immediately rejected by their non-ADHD peers; for example, by the end of their first play session (Erhardt and Hinshaw 1994; Mrug et al. 2001). Once peer rejection develops within a social group, it is highly resistant to change (Murray-Close et al. 2010). Longitudinal data from the MTA study showed vicious cycles between aggression and social skills and between peer rejection and social skills (e.g., aggression at Time 1 → lower social skills at Time 2 → heightened aggression at Time 3 → lower social skills at Time 4) (Murray-Close et al. 2010). These reinforcing cycles of dysfunction may contribute to accumulating difficulties faced by children with ADHD. Unfortunately, peer problems can follow children with ADHD wherever they go (Mrug et al. 2007). The evidence is overwhelming that peer rejection in ADHD is pervasive and stable over time, persisting from childhood at least into adolescence (Johnston et al. 1985; Bagwell et al. 2001). Moreover, peer rejection in ADHD children is highly impairing, as shown in the MTA study in which peer rejection independently predicted cigarette smoking, delinquency, anxiety, and global impairment at 6 year post-baseline (average age, 15 years) and global impairment at 8 years (average age, 17 years) (Mrug et al. 2012).

Although attention problems and nonaggressive externalizing behaviors (e.g., restlessness, intrusiveness) may contribute to peer problems (Nijmeijer et al. 2008) IA versus instrumental aggression has been most strongly implicated in terms of peer rejection. Impulsively aggressive children are less accepted and experience greater rejection and victimization than peers who are nonaggressive or engage in instrumental aggressive acts (Boivin et al. 1995; Card et al. 2006; Morrow et al. 2006; Evans et al. 2015). In fact, children in whom aggressive acts are primarily instrumental are more likely to be popular with peers (Boivin et al. 1995; Card et al. 2006; Evans et al. 2015). Impulsive aggression has also been associated with fewer friendships and lower quality/higher conflict friendships (Poulin and Boivin 2000; Abikoff et al. 2004; Evans et al. 2015).

Evans et al. (2015) examined the relative roles of IA and instrumental aggression in the association between ADHD symptoms (inattention, hyperactivity-impulsivity) and peer rejection in adolescence. Results showed that hyperactivity-impulsivity was uniquely linked with IA, which was in turn predictive of peer rejection. In contrast, hyperactivity-impulsivity was predictive of instrumental aggression but instrumental aggression was not uniquely associated with peer rejection. The specific path of hyperactivity-impulsivity → IA → peer rejection accounted for two thirds of the total variance in the model. Because hyperactive-impulsive youth who engage in impulsively aggressive behavior are at especially high risk of peer problems/social maladjustment, timely intervention with effective treatments targeting hyperactivity-impulsivity and IA might lead to improving social outcomes driven by peer rejection (Jensen et al. 2007; Evans et al. 2015)

Pharmacotherapy in Impulsive Aggression Associated with ADHD

The ultimate goal of intervention in children with ADHD is to minimize or eliminate functional impairment caused by the disruptive effects of ADHD on psychosocial development. The finding that ADHD-related impairment is attributable more to aggression/irritability than to ADHD symptoms themselves (Jensen et al. 2007) emphasizes the need to target aggression in ADHD with evidence-based treatment strategies.

Current treatment recommendations in children with ADHD and comorbid IA are to first treat the primary disorder – ADHD – before directly targeting IA, with the idea that successful treatment of ADHD will have a positive impact on associated disruptive behaviors such as IA (Pappadopulos et al. 2003; Steiner et al. 2003; Connor et al. 2006; Jensen et al. 2007). Various guidelines have outlined systematic approaches relevant to the assessment and management of ADHD and IA (Pappadopulos et al. 2003; Pliszka et al. 2006; Pliszka and AACAP Work Group on Quality Issues 2007; Wolraich et al. 2011; Scotto Rosato et al. 2012). Across guidelines, psychosocial intervention with an effect size of 0.4–0.9 (Connor et al. 2006) is an important backdrop to pharmacotherapy. Its initiation relative to pharmacotherapy is based on considerations such as symptom severity and family preferences/concerns.

A number of stimulant and nonstimulant medications have been approved by the United States Food and Drug Administration for the management of ADHD in children and adolescents based on double-blind, randomized, placebo-controlled trials demonstrating significant reductions in core ADHD symptoms as well significant improvements in global outcome assessments. Guidelines universally recommend that ADHD-directed pharmacotherapy be initiated with one of these medications as monotherapy, which should be tailored to individual needs for optimal balance of improvement and tolerability.

An abundance of empirical evidence supports that psychosocial/behavior therapy plus medication monotherapy should be the primary therapy for children with ADHD. The recommended ''next step,'' when clinically significant aggression persists despite ADHD monotherapy, is to specifically target aggression with a different class of medication (Pappadopulos et al. 2003; Pliszka et al. 2006; Pliszka and AACAP Work Group on Quality Issues 2007; Scotto Rosato et al. 2012). However, no medication has yet been approved for the management of IA, whether globally across psychiatric disorders or as an element of a specific disorder. Guidelines relevant to pharmacotherapy in children with ADHD and comorbid aggression have been disadvantaged by the paucity of data from randomized controlled trials that specifically assessed aggression as a primary outcome in ADHD children. Because the body of empirical evidence supporting combination therapy in children with ADHD and IA remains extremely limited, the 2007 Consensus Report on IA (Jensen et al. 2007) has spurred efforts to address the treatment needs of this vulnerable, at-risk population.

ADHD-targeted monotherapy: Effect on IA

Numerous studies have demonstrated that primary ADHD therapy reduces not only core ADHD symptoms but also symptoms of comorbid disruptive behavior disorders (Connor et al. 2010b). However, few studies have assessed the impact of ADHD medications on aggression *per se*, much less on IA. Most studies have used instruments that broadly assessed disruptive behaviors across heterogeneous domains such as oppositionality/irritability/aggression, or have not separated IA from instrumental aggression, which may be less medication responsive.

In meta-analyses collating data from studies with stimulants in children and adolescents with ADHD with or without CD or ODD, mean effect sizes for overt aggression ranged from 0.60 (Scotto Rosato et al. 2012) to 0.84 (Connor et al. 2002), compared with 0.77–1.2 for core ADHD symptoms (Faraone and Buitelaar 2010). Just as nonstimulants (α-2 agonists, atomoxetine) have more modest effect sizes relative to stimulants in core ADHD symptoms (e.g., $\sim$0.6), effect sizes for disruptive behaviors in ADHD are also somewhat smaller for nonstimulants relative to stimulants (e.g., $\sim$0.3–0.4) (Hirota et al. 2014; Schwartz and Correll 2014).

Despite the relatively robust effects of stimulants on externalizing behaviors/aggression, an exploratory post-hoc analysis of data from the MTA study demonstrated the limits of stimulant monotherapy (Jensen et al. 2007). In children with moderate or high baseline levels of aggression who were assigned to medication alone or in combination with behavior therapy, 44% still had significant impairment caused by aggressive behaviors at 14 months, even though medication was tightly monitored to maintain optimal dosages. A more recent study prospectively examined the impact of stimulant therapy in preadolescent children with ADHD and comorbid ODD or CD who presented with marked, persistent aggression despite previous treatment with a stimulant (Blader et al. 2010). Once stimulant monotherapy was optimized, 50% of patients still had clinically significant aggression. Given the potent effect of aggression on ADHD outcomes, these observations make clear why long-term outcomes improve with primary ADHD therapy but not to the level of children without ADHD.

Aggression-targeted combination therapy

Although children and adolescents with stimulant-refractory aggression may represent a relatively small subset of youth with ADHD, they are an especially vulnerable, at-risk population who bear the brunt of ADHD-related morbidity. These patients may benefit from the addition of a drug of a different class to manage residual aggressive behaviors refractory to primary ADHD therapy.

Antipsychotics, mood stabilizers, and α-2 agonists have been evaluated, at one time or another, for their effects on aggression in children. Although risperidone and other ''atypical'' antipsychotics have historically been at the forefront of treatment recommendations regarding combination therapy for managing comorbid aggression in children with ADHD (Pappadopulos et al. 2003; Pliszka et al. 2006; Pliszka and AACAP Work Group on Quality Issues 2007), only two double-blind randomized placebo-controlled trials of risperidone as adjunctive therapy in children with ADHD and stimulant-resistant aggression have been published: 1) A pilot study in 25 children that was likely underpowered and did not detect a significant treatment effect (Armenteros et al. 2007; Aman et al. 2014), and 2) the recently completed Treatment of Severe Childhood Aggression (TOSCA) study in which the effect size for IA as a secondary end-point was modest (0.29) (Farmer et al. 2011; Aman et al. 2014; Gadow et al. 2014). The TOSCA study has provided at least some initial empirical evidence to support a stepped-care approach in which ADHD children with severe aggression are initially treated with primary ADHD therapy (medication plus parent training) followed by adjunctive antipsychotic therapy targeted to IA. However, the long-term cardiometabolic effects of risperidone and similar antipsychotics, especially in the face of very limited evidence of efficacy as IA-targeted therapy in ADHD, have become cause for considerable concern. Despite opposing effects on weight, stimulant cotherapy does not attenuate the adverse effects of risperidone or similar agents on body composition, metabolic parameters, prolactin, or sedation (Calarge et al. 2009; Penzner et al. 2009). Although metabolic profiles may differ across atypical antipsychotics, all are associated with significant weight gain and shifts to overweight or obese status (Correll et al. 2009), underscoring the need to consider weight and metabolically neutral alternatives as IA-targeted therapy.

Clinical research on the use of ''typical'' antipsychotics to target aggressive behaviors in in children and adolescents was essentially abandoned once newer antipsychotics became available, out of the now mistaken belief that the risk of extrapyramidal side effects (EPS) was significantly lower with the newer agents and that children were more susceptible to EPS occurrence (Pappadopulos et al. 2003), However, EPS incidence and changes in EPS ratings have been shown to not be significantly different when directly comparing atypical antipsychotics with atypical antipsychotic of intermediate potency (Miller et al. 2008). This has led to a more nuanced picture of antipsychotics as a single drug class with a spectrum of EPS risk that depends largely upon dopamine- and acetylcholine-receptor binding affinities as well as individual susceptibility (Caroff et al. 2011), and to an interest in the potential role of midpotency weight and metabolically neutral antipsychotics as IA-targeted therapy in children and adolescents with ADHD.

Published data on such drugs as adjunctive therapy in stimulant-refractory aggression are limited to an open-label, dose-ranging study with an experimental formulation of molindone (Stocks et al. 2012), which showed dose-related improvements in oppositional behaviors/conduct problems in preadolescent ADHD children with serious conduct problems and aggressive behavior. Results of a subsequent double-blind, placebo-controlled study (NCT01364662) in children with IA associated with ADHD have not yet been published. However, in a double-blind study in schizophrenic youth, molindone appeared to be a potentially promising alternative given its favorable safety profile relative to atypical antipsychotics (Sikich et al. 2008). Contrary to expectations at the time the study was initiated, the antipsychotics molindone, olanzapine, and risperidone could not be differentiated on the basis of efficacy or tolerability (i.e., discontinuations caused by adverse effects); however safety profiles were significantly different at the doses used to treat schizophrenia. Olanzapine and risperidone, but not molindone, were associated with significant increases in weight/body mass index (BMI). Whereas akathisia was reported by more molindone-treated patients, it was not associated with more dystonic or parkinsonian symptoms than the comparators (prophylactic benztropine used in all groups). As the study authors noted, different adverse effect profiles are difficult to rank in terms of their clinical importance, but the profile for antipsychotics with adverse weight and metabolic effects represents a cardiovascular safety concern, whereas the concern with molindone in terms of akathisia/EPS may be one of tolerability/adherence (Sikich et al. 2008).

Mood stabilizers and the α-2 agonists clonidine and guanfacine are also drugs of interest as adjunctive therapy in children with ADHD and severe aggression/disruptive behavior disorders. A double-blind, placebo-controlled trial with divalproex is particularly informative in that it assessed treatment effects using an aggression-specific instrument (Retrospective Modified Overt Aggression Scale [R-MOAS]) albeit without differentiating impulsive from instrumental aggression (Blader et al. 2009). By showing that the proportion of patients in whom aggression remitted (i.e., behaviors markedly more manageable and not requiring further changes in pharmacotherapy) significantly favored adjunctive therapy (divalproex) over stimulant monotherapy (placebo), this study provides support for a stepped-care approach to drug therapy in children with ADHD and severe IA. Larger studies with divalproex as well as other classes of drugs are needed to replicate the findings. In addition, long-term follow-up is needed to determine that normalizing IA behavior in children with ADHD has additive benefit in terms of improving long-term outcomes.

Conclusions

For many children with ADHD, symptoms eventually remit with effective intervention. However, the prospects are very different for children in whom ADHD is marked by chronic aggression, especially IA. They struggle to navigate the demands of daily living, particularly those related to social function. Their behavior is anathema to peers, which can initiate a vicious cycle of escalating dysfunction. Current treatment recommendations for these children involve a stepped-care approach with intervention that initially targets ADHD, followed by the addition of a non-ADHD medication targeting residual IA. Although primary ADHD therapy is supported by a large body of empirical evidence, clinicians do not yet have empirical data to support decisions on which IA-targeted drug to use, when to initiate adjunctive therapy, how to monitor progress, or when to change or discontinue medications. However, with IA in childhood ADHD now being recognized as a serious clinical and public health concern, research efforts are underway to address the need for effective treatments in this high-risk population.

Clinical Significance

In the clinic, physicians encounter IA as a relatively common comorbidity of ADHD in children and adolescents. The presence of IA in association with ADHD does not imply or require a comorbid diagnosis of ODD, although the approach to management may be similar. Impulsive aggression should be viewed as a marker of severe disease that amplifies the negative consequences of ADHD and, therefore, requires timely and intensive intervention. In the current recommended stepped-care approach, the first step is ADHD-targeted therapy, which should then be followed by specific aggression-targeted therapy if aggressive behaviors do not remit. However, clinicians should recognize that empirical evidence is still lacking as to aggression-targeted treatments with favorable benefit–risk profiles for children and adolescents with ADHD and severe aggression.

Acknowledgments

The authors received editorial assistance with manuscript preparation from Alan Blackburn and Verna Ilacqua, ID&A.

Disclosures

Dr. Saylor receives clinical trial research support from Alcobra, Eli Lilly, Neurovance, Otsuka, Purdue, Shire, and Supernus. He serves as a consultant and advisory board member for Supernus and Neurovance. Dr. Amann serves as a speaker and/or consultant for Actavis, Otsuka, Pfizer, Rhodes, Shire, Supernus, and Takeda/Lundbeck.

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