Juvenile Maladaptive Aggression: A Review of Prevention, Treatment, and Service Configuration and a Proposed Research Agenda

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Objective: To review prevention programs, psychosocial and psychopharmacologic treatments, and service delivery configurations for children and adolescents with maladaptive aggression. To propose a research agenda for disorders of aggression in child and adolescent psychiatry.

Data Sources: Recent empirical studies were reviewed using searches of MEDLINE and PsycINFO (text terms: *aggression*, *antisocial*, *violence*, *conduct*, *oppositional*, *psychosocial treatment*, *psychopharmacology*, and *prevention*), relevant books, review articles, and bibliographies.

Data Extraction: Articles met the following criteria: published in an English-language, peer-reviewed journal between 1980 and 2005, included a focus on individuals < 18 years old, and included an outcome measure of relevant significance.

Study Selection: Results of 154 randomized, controlled psychosocial treatment trials, 20 controlled psychopharmacology studies, 4 open-label medication studies, and 2 psychopharmacology meta-analyses were reviewed.

Results: Prevention programs show promise for reducing future aggression in at-risk populations. Empirical support is available for the effectiveness of multifocused psychosocial treatments in reducing aggression in children and adolescents. Atypical antipsychotics, lithium, divalproex sodium, and stimulants for conduct problems associated with attention-deficit/hyperactivity disorder have empirical support for reducing aggression in selected patient populations.

Conclusions: Therapeutic nihilism in the treatment of aggressive children and adolescents with conduct problems is no longer warranted. Multifocused psychosocial interventions given early in life to at-risk children have the most support for effectiveness. However, treatments for children who routinely present to the child psychiatrist with already well-established disorders of aggression are neither robust nor well-established. Further research into maladaptive aggression in referred children and adolescents within and across psychiatric diagnoses is important for the field of child and adolescent psychiatry.

(J Clin Psychiatry 2006;67:808–820)

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No external funding was utilized in support of this review.

Financial disclosure appears at the end of this article.

We thank the following expert reviewers: Alan E. Kazdin, Ph.D., Yale University School of Medicine, New Haven, Conn., and Karen D. Wagner, M.D., Ph.D., University of Texas Medical Branch, Galveston.

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This article is designed to review treatments for aggression, conduct problems, antisocial behaviors, and violence in children and adolescents and to propose directions for future research. Data from prevention research, and the current status of psychosocial and psychopharmacologic interventions for maladaptive aggression in child and adolescent psychiatry, are reviewed. Service configuration models to best serve these children and adolescents are discussed. Finally, a research agenda for disorders of excessive maladaptive aggression in children and adolescents is proposed.

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Problems with aggression and conduct in children and adolescents are not new. Reviews of treatment research conducted in the 1960s, 1970s, and 1980s were decidedly pessimistic and documented a lack of treatment efficacy for aggressive children with conduct problems.[1,2] Many clinicians wondered whether it was at all possible to intervene effectively for children and adolescents diagnosed with conduct disorder (CD). Psychiatric interventions, largely based on psychoanalytic principles and psychological treatments given singly and sequentially in isolation, did not seem to work for these children and adolescents. Early research had yet to elucidate the importance of developmental psychopathology in the etiology of early-onset CD, nor did clinicians appreciate the need for multimodal interventions applied concurrently, as opposed to single interventions applied in isolation, in the treatment of aggressive and antisocial children and adolescents. Although most contemporary clinicians would agree that robustly effective treatments are still lacking for CD and other forms of aggressive and antisocial behaviors in children and adolescents, such behaviors are now viewed by clinicians as partly modifiable.[3–5]

Aggression may be defined as any behavior that is intended to be destructive to the self, others, or objects and property.[6] Maladaptive aggression is behavior that, by virtue of its intensity, frequency, and/or duration, is not adaptive for the individual, is out of proportion to the usual eliciting environmental precipitants, violates societal rules, and is the expression of a disordered internal central nervous system mechanism such as that which occurs in the context of psychiatric disorders.[3,7] Maladaptive aggression falls into 2 broad categories: premeditated, instrumental, predatory aggression and reactive, impulsive, defensive, affective aggression.[7] These behaviors may occur across many diagnoses in clinically referred children and are not confined to the psychiatric diagnoses of CD or oppositional defiant disorder (ODD).[8]

Maladaptive aggression in children and adolescents represents a significant public health problem in the United States. Indeed, acute and chronic aggressive behaviors are a frequent reason for clinical referral to child and adolescent psychiatrists working in a wide variety of settings, including ambulatory psychiatry clinics, where up to 60% of the referrals are for evaluation and treatment of aggressive children and adolescents.[3,4,9,10] Violence is a predictor of urgency in pediatric emergency psychiatric settings, accounting for 62% of child and 32% of adolescent psychiatric emergency visits.[11] In a survey study, only 4% of 515 staff from 15 child/adolescent/adult inpatient units reported no impulsive aggression on their wards over a period of 6 months, and about a third reported seeking medical attention (first aid) for a patient-related assault injury.[12] Clinically referred children and adolescents exhibit a significant frequency of severe aggression in the 6 months prior to child psychiatric referral, regardless of diagnosis.[8] Overall, excessive, maladaptive, and impulsive aggression in the clinical setting consumes an enormous quantity of resources and is frequently refractory to standard treatment interventions.

METHOD

A search for relevant literature was conducted via MEDLINE and PsycINFO using the following text terms: *aggression*, *antisocial*, *violence*, *conduct*, *oppositional*, *psychosocial treatment*, *psychopharmacology*, and *prevention*. Selected bibliographies were accessed in published books and review articles. Only results from randomized, controlled trials (RCTs) were included for psychosocial treatments. (We reviewed 154 trials.) Because the pediatric psychopharmacology literature is so thin in this area, 4 open-label medication trials and 2 meta-analyses, in addition to 20 randomized studies, were also included. To be included, articles met the following additional criteria: published in an English-language, peer-reviewed journal between 1980 and 2005, included a focus on individuals < 18 years old, and included an outcome measure of relevant significance.

PREVENTION AND PSYCHOSOCIAL TREATMENTS

Early Intervention Programs

The 1970s and 1980s saw the development and implementation of a variety of early intervention programs for at-risk, generally impoverished children. These programs were not developed specifically to address childhood aggression and antisocial behaviors. Rather, their goal was to promote adaptive social functioning in children by providing a mix of child care, family support, parental educational and job training, parent child education and parent management training (PMT), and preschool education to high-risk families with children 0 to 5 years old. These broad, early intervention programs may have long-term effects on reducing the occurrence of conduct problems.[13–17] Long-term effects have been noted later in childhood and adolescence and, in at least 2 programs, into adulthood.[13,18] Their effect sizes are medium to large, ranging from 0.42 to 1.1.[15,16] These outcomes are of particular interest, because the prevention of conduct problems and antisocial behavior was not a stated goal of these early intervention programs (see Table 1).

Prevention Programs Targeting the Onset of Child Aggression, Conduct Problems, and Antisocial Behaviors

Based on findings from early intervention programs, programs specifically designed to prevent the onset of childhood aggression and conduct problems in at-risk children and families were developed (see Table 2). These programs are expensive, generally require governmental

Table 1. Empirically Validated Primary Prevention Programs That Had a Later Impact on the Development of Child Aggression, Conduct Problems, and Antisocial Behaviors

Program	Age of Children, y	Intervention Format	Program Frequency	Program Duration, y	Outcomes
Chicago Child-Parent Center[13]	3–9	Comprehensive educational services, family services, health services	Daily to weekly	1–2	↓ arrest rates at 15-year outcome
High Scope Perry Preschool Project[18]	3–4	Classroom: academic skills training, child skills training, parent skills training, home visitation	Daily	Academic year	↓ arrests and ↓ delinquency at 27-year outcome
Houston Parent Child Development Center[104]	1–3	Home visits, parenting support and education, child care, weekend workshops with fathers and siblings	Weekly	2	↓ conduct problems at 7-year outcome. Results no different than controls at 15-year outcome
Syracuse University Family Development Project[105]	0–4	Home visits, parenting support and education, stress coping, child care, case management	Weekly	4.5	↓ arrests and ↓ delinquency at 10-year outcome
Yale Child Welfare Research Program[17]	0–2.5	Home visits, parenting support and education, stress coping, child care, case management	Weekly	2.5	↓ aggression at 10-year outcome

Symbol: ↓ = decreased.

Table 2. Empirically Validated Multifocused Intervention Programs Designed to Prevent the Onset of Child Aggression, Conduct Problems, and Antisocial Behaviors

Program	Age of Children, y	Intervention Format	Program Duration, wk	Outcome
Fast Track Conduct Problems Prevention Research Group[106–108]	6–12	Classroom-based child skills training, home-based individual parent skills training, child academic supports, group parent training	312	↓ conduct problems
First Step[109]	5	Home-based parent skills training, group child skills training, access to program consultants	6	↓ aggression
Incredible Years Teacher Training[27]	4–8	Group teacher training, group parent training, child skills training	50	↓ classroom aggression, ↓ conduct problems at home
Linking the Interests of Family and Teacher[110]	7–11	Group parent skills training at school, classroom-based child skills training, playground program	10	↓ physical aggression
Montreal Program[111]	7–9	Child social skills training, home-based individual parent skills training	19	↓ conduct problems
Seattle Social Development Project[112,113]	7–11	Child academic, social skills, problem-solving skills training, optional parent skills training	260	↓ violence at age 18, ↓ aggression

Symbol: ↓ = decreased.

financial support, are generally implemented in the early elementary school years, are given continuously over a period of 2 to 5 years, have a community focus, deliver multiple psychoeducational treatment interventions in a single package, and share a broad goal of skill-building (i.e., increasing social competence, enhancing prosocial problem-solving skills, and increasing resilience).

Results of programs specifically designed to prevent the onset of childhood aggression and antisocial behaviors show that they generally are effective, with long-term benefits in reducing antisocial behaviors, delinquency, CD, and substance use initiation in at-risk children over follow-up periods lasting several years (Table 2). However, not all secondary prevention programs for conduct and antisocial problems proved successful.[19] Successful programs typically include (1) multimodal interventions that simultaneously target the child and family, parent supports, teacher involvement, and early childhood education (interventions with only a single focus appear much less effective); (2) intensive interventions generally delivered on a daily to weekly basis; (3) sufficient duration of intervention, generally 2 years or longer; (4) use of specific interventions empirically shown to be effective in ameliorating known psychosocial mechanisms that increase risk for conduct problems (e.g., coercive family process, harsh and inconsistent parental discipline, failure of parents to monitor the whereabouts of older children); (5) child and parent interventions that emphasize skill-building, problem-solving, and coping skills; (6) interventions that begin early in a child's life (between 0 and 6 years old); (7) individual case management; and (8) intensive collaboration among community, juvenile justice, school, family, and mental health professionals. Prevention programs that have these characteristics appear to reduce aggression and conduct problems during child development.

Another approach is to emphasize violence prevention in the school.[20] For children and adolescents who demon-

Table 3. Empirically Validated Psychosocial Programs Designed to Prevent the Onset of Child Aggression, Conduct Problems, and Antisocial Behaviors

Program	Age of Children, y	Intervention Format	Program Duration, wk	Outcome
Skill-building interventions				
Earlscourt Social Skills Program[114]	6–12	Small group: child skills training, parent skills training	15	↓ aggression
Incredible Years Dinosaur Program[27]	4–8	Small group: child skills training	40	↓ peer aggression
Peer coping skills training[115]	6–8	Small group: child skills training	22	↓ aggression
Problem-solving curriculum[44]	7–13	Individual: parent and child skills training	25	↓ conduct problems at age 11
Social skills training[116]	9–13	Small group: social cognitive skills training	11	↓ aggression
Parent- and family-focused interventions				
Community-based program[117]	2–5	Group: parent skills training	24	↓ child behavior problems
DARE to be You[118]	2–5	Group: parent skills training	24	↓ child oppositional behaviors
Enhanced family treatment[119]	4–9	Individual: family skills training	25	↓ child conduct problems
Helping the Noncompliant Child[120]	3–8	Individual: parent skills training	12	↓ child noncompliance
Home visiting[121]	Infants	Individual: parent education	78	↓ aggression at age 5
Home visiting[122]	Prenatal and infants	Individual: parent education	52	↓ child arrest at age 15
Incredible Years Parenting Program[27]	2–8	Group: self-administered parent skills training	15	↓ child conduct problems
Living with Children[35]	3–12	Family skills training	20	↓ child conduct problems
Parent-Child Interaction Therapy[123]	2–6	Individual: parent and child skills training	14	↓ child conduct problems
Positive Parenting Program[124]	7–14	Individual: self-administered parent skills training	12	↓ child conduct problems
Structural family therapy[42]	6–12	Individual: family	20	↓ child conduct and behavioral problems
Synthesis Training[125]	5–9	Individual: parent skills training	36	↓ child aversive behaviors

Abbreviation: DARE = Decision-making, reasoning skills, and problem-solving; Assertive communication and social skills; Responsibility (internal locus of control/attributions) and role models; Esteem, efficacy, and empathy.
Symbol: ↓ = decreased.

strate aggressive and violent behavior in the school setting, the results of a meta-analysis of 44 school-based violence prevention programs had effect sizes ranging from 0.36 to 0.59.[21]

Psychosocial Programs Designed to Prevent or Treat Child Aggression, Conduct Problems, and Antisocial Behaviors

Research has elucidated specific moderators and mediators of psychosocial treatment response for disorders of maladaptive aggression. Moderators identify on whom and under what circumstances treatments have different effects (i.e., initial conditions). Mediators identify why and how treatments have effects (e.g., mechanisms of treatment).[22] Significant patient moderators include younger child age, greater chronicity and severity of symptoms, lower verbal IQ, and pervasiveness of family psychopathology. Treatment moderators include comprehensiveness of the intervention, treatment duration, and ability to target multiple domains of impairment.[3,4,23–27]

Three well-studied mediators of early-onset aggression and conduct problems include coercive family processes,[28] other parent practices, and deficient social skills. The first mechanism describes how parents and children train each other through the mechanism of mutual negative reinforcement to become oppositional and aggressive as a way of escaping aversive interpersonal situations. This learning may then generalize out of the home as the child develops and may facilitate a developmental trajectory toward ODD or CD. Other parenting practices associated with the development of antisocial behaviors include lack of parental monitoring of the child's whereabouts and friendships, low nurturing and engagement in the child's daily life, and harsh and inconsistent discipline.[29,30] Enhanced social skill-building and conflict-resolution skills in aggressive families may function as a mediator of treatment.[31] Dodge and colleagues[32] have described specific skill deficits from which aggressive children misinterpret neutral environmental stimuli as threatening and then react aggressively.

As a result of this research, psychosocial treatments emphasize PMT and individual skill-building approaches (Table 3). PMT teaches consistent parenting, positive and less harsh discipline practices, monitoring of the child, and positive feedback for the child.[14] A variety of programs have been developed and tested against control conditions.[33–38] In general, these parent-training programs appear effective in decreasing young children's oppositional, defiant, noncompliant, and aggressive behaviors.[39] Several family therapy programs, such as functional family therapy, have been found promising.[40–43] Unfortunately, work conflicts, life stress, personal psychopathology, or lack of motivation often preclude parent participation in treatment.

Table 4. Empirically Validated Multifocused Intervention Programs Designed to Treat Already Established and Chronic Adolescent Violent and Criminal Juvenile Offenders

Program	Age of Children, y; Status	Intervention Format	Program Duration, wk	Outcomes
Coping Course[126]	12–22; incarcerated	Group: skills training	8	↓ conduct problems while in detention
Multidimensional Treatment Foster Care (MTFC)[52,53]	12–17; serious offenders	MTFC: family skills training; individual skills training; intensive supervision at home, community, school; psychiatric consultation and medication management as needed; community liaison; case management	12–26	↓ criminality and violence at 18-month outcome
Multisystemic Treatment (MST)[23,24,26,57]	12–17; serious offenders	MST: individual skill training; parent skill training; family, community, school collaborative interventions; intensive case management	10–15	↓ arrest rates at 4-year outcome[23,24]; ↓ arrest rates, ↓ conduct problems[26,57]

Symbol: ↓ = decreased.

Skills-training approaches focus on the individual child. These programs emphasize social skills, problem-solving techniques, and anger management strategies in reducing child aggression and conduct problems[27,44,45] and individual therapy approaches based on the principles of cognitive-behavioral therapy (CBT).[46] However, there may be limited generalizability of treatment benefits once treatment is completed.[27,47]

This specificity has led to the development of multifocused psychosocial programs for child conduct problems (Table 3).[27,48] These programs combine PMT, structural family therapies, and child skill-building treatments. The overall effect size of multifocused psychosocial treatment programs on preventing the worsening of conduct problems and aggression in at-risk children is medium to large, ranging from 0.4 to 0.9[27,47,48] Many of these programs demonstrate lasting effects after treatment is completed.[45,49]

Intervention Programs Designed to Treat Chronic Violent Juvenile Offenders

Multisystemic Treatment (MST) and Multidimensional Treatment Foster Care (MTFC) are programs that have been developed to treat older children and adolescents with aggression necessitating juvenile justice involvement.[23,50–52] These programs are designed as alternative placements to incarceration or psychiatric hospitalization and encompass a variety of psychoeducational, community, and mental health services (Table 4). MST and MTFC have demonstrated effectiveness in the treatment of severely disturbed families and violent adolescents, reporting decreased arrest rates ranging from 25% to 70% over 1- to 4-year outcomes.[24,53] As such, these programs appear promising in the treatment of severely aggressive adolescents with chronic juvenile justice histories.

Limitations of Psychosocial Treatment Programs

Limitations of extant treatment programs for children and adolescents with excessive, maladaptive aggression are several. First, the effect size of well-validated PMT programs appears inversely related to age[3] and declines with increasing age.[33] Second, after therapy is completed, the temporal generalizability of treatment effects appears low.[4] Beneficial effects of the therapy often do not appear to generalize beyond the therapy setting. Third, CBT effects vary with age. A meta-analysis of CBT for aggression reported effect sizes of 0.9 for older children (ages 11–13 years) but of only 0.5 for younger children (e.g., for ages 5–7 years, effect size = 0.57; for ages 7–11 years, effect size = 0.55).[46] Fourth, individual and family therapy programs often assume that parents are generally free of psychopathology. Given the heritability and nongenetic familial aggregation rates for most psychiatric disorders, this assumption may not be met. As such, parental psychopathology may diminish the effectiveness of PMT and family interventions.[4] Fifth, dropping out of psychosocial therapies is a significant problem. Among individuals who begin therapy, rates of premature dropping out range between 30% and 60%.[54,55] Rates of premature therapy termination for aggressive children with antisocial and oppositional behaviors hover around 50%.[4,54] Unfortunately, the same correlates that increase risk for aggression and conduct problems also increase risk for premature therapy termination. These include family structures characterized by single parents, younger mothers, homes headed by a nonbiological parent, chronicity and severity of aggressive symptoms before treatment initiation, contact with antisocial peers, receipt of public assistance, and low child verbal IQ. As the frequency, severity, and intensity of psychopathology deepen in the child, adolescent, and family system, therapy response rates generally diminish.[5,56]

In summary, prevention programs and multifocused psychosocial approaches to disorders of maladaptive aggression are the best-studied treatments to date. For empirically based psychosocial treatments, effect sizes appear to range from 0.4 to 0.9, depending on the specific type of treatment, the age of the child, and other treatment moderators and mediators, at least in

the short run.[3] At present, research supports PMT, behavioral approaches, skill-building therapies, CBTs, and broad, multimodal wraparound services as more effective psychosocial interventions for aggressive children and adolescents than individual or group psychodynamic or traditional unfocused and open-ended psychotherapy approaches.[3,4,57] Nevertheless, there exist limitations to these interventions.

PSYCHOPHARMACOLOGY

Psychopharmacologic treatment of early-onset, excessive maladaptive aggression has also advanced over the past 2 decades. These approaches are as yet adjunctive to comprehensive psychosocial, community, and psychoeducational interventions. This relationship may change, however, as both preclinical and clinical research have begun to reveal the underlying neurobiological mechanisms that modulate agonistic aggressive responding,[6,58] allowing for more effective treatments.

Moderators and mediators of psychopharmacologic effects on maladaptive aggression have yet to be elucidated. Aggression may be a nonspecific symptom associated with a wide variety of clinical psychiatric disorders.[6,59–61] This relationship may be moderated or mediated in part by impulsivity[62,63]; negative emotions such as hostility,[64] irritability,[65] fear, and acute stress[66]; and/or lack of empathy for the suffering of others.[67] Type of aggression may be an important moderator of outcome in the pharmacologic treatment of aggression. While psychosocial interventions may theoretically be effective for both proactive and reactive aggression, psychopharmacology appears more effective for reactive types of aggression[7] The role of neurobiological variables, their responsiveness to psychopharmacologic intervention, and the interaction of neurobiological and psychosocial variables in mediating the outcomes of psychopharmacologic treatment interventions remain to be explored.

Psychopharmacologic interventions are generally palliative in disorders of maladaptive aggression. Pharmacologic approaches are either disorder-oriented or target-symptom–oriented. The disorder-oriented approach seeks to treat the specific underlying psychiatric disorder for which maladaptive aggression is one associated symptom, theorizing that successful treatment of the primary disorder should ameliorate associated aggression. The target-symptom approach seeks to medicate aggressive behavior directly, regardless of the underlying psychiatric condition. It is currently recommended that the primary disorder be treated first, before adopting the target symptom approach.[3,7]

While patients with ODD and CD can improve with pharmacotherapy,[68] these disorders are generally not considered robustly medication-responsive conditions. Thus, accurate identification and treatment of medication-responsive comorbid diagnoses is important (e.g., attention-deficit/hyperactivity disorder [ADHD], depression, bipolar disorder, and anxiety disorders). Target-symptom approaches to medicating ODD and CD should be initiated only after the environmental context in which they occur is fully appreciated and behavioral therapies, skill-building therapies, parent management interventions, and attempts to increase environmental structure and monitoring of the child have failed.[69–71]

Atypical Antipsychotics

Second-generation antipsychotics (i.e., atypical antipsychotics) show substantial efficacy for treating aggression in selected samples.[71] Risperidone is the best studied, although its mechanism of action for reducing aggression is unclear (Table 5). Randomized, placebo-controlled clinical trials find it to be effective in reducing aggression in children and adolescents with CD,[68] disruptive children with subaverage IQ,[72–77] and children with autism.[78] Aggression in these studies was defined on dimensional measures, and efficacy was generally defined as a 25% to 50% reduction in symptoms. Risperidone doses ranging from 0.25 to 3.0 mg/day in divided doses were generally well-tolerated. Three long-term studies reported that risperidone continued to be well-tolerated and effective in children with below-average IQ up to 52 weeks.[76,79,80] All extant RCTs investigating the effects of risperidone on aggression in children and adolescents have yielded positive outcomes, suggesting fairly robust treatment effects for maladaptive aggression. Other atypical antipsychotics, such as olanzapine, quetiapine, ziprasidone, and aripiprazole, have yet to be examined under controlled conditions for disorders of maladaptive aggression in children and adolescents. An open-label study found clozapine effective in reducing aggression in children and adolescents with schizophrenia.[81]

Neuroleptics

First-generation antipsychotics found effective in reducing aggression in CD include molindone[82] and haloperidol.[83] However, concerns about side effects preclude their being recommended at this time.[70]

Mood Stabilizers

Lithium and divalproex sodium have been found effective in reducing aggression in children and adolescents with CD.[7,84–86] Notably, controlled studies indicate that mood stabilizers may be more effective for reducing explosive aggression in CD than in treatment of early-onset bipolar disorders. The exception is carbamazepine, which was not more effective than placebo in treating aggression in children with CD.[87] A randomized, controlled study of valproate for aggression in children and adolescents with pervasive developmental disorders was nega-

Table 5. Recent Controlled Studies of Medications for Aggression and Disruptive Behavioral Symptoms in Children and Adolescents

Study	Diagnosis/ Symptoms	Study Type	N	Age, mean or range, y	Drug	Dose	Duration, wk	Outcome
Anticonvulsants								
Cueva et al (1996)[87]	CD	RCT	22	9	Carbamazepine	400–800 mg/d, mean serum level = 6.8 μg/mL	6	CBZ = placebo
Donovan et al (2000)[85]	CD/ODD	CO	20	10–18	Divalproex	750–1500 mg/d, mean serum level = 82.2 μg/mL	12	↓ CD/ODD symptoms
Steiner et al (2003)[127]	CD	RCT	58	16	Divalproex	High dose (500–1500 mg/d)	8	↓ CD symptoms
Hellings et al (2005)[88]	PDD	RCT	30	6–20	Valproate	Level 77.8 μg/mL	8	VPA = placebo
Antidepressants								
Gordon et al (1993)[128]	PDD + anger	CO	24	6–23	Clomipramine	Mean dose = 152 mg/d	10	↓ anger attacks, severe side effects
Atypical antipsychotics								
Aman et al (2002)[72]	MR + DBS	RCT	55	5–12	Risperidone	Mean 1.16 mg/d, 0.006–0.092 mg/kg/d	6	↓ CD symptoms
Buitelaar et al (2001)[73]	MR + DBS	RCT	38	12–17	Risperidone	1.5–4 mg/d	6	↓ aggression
Findling et al (2000)[68]	CD	RCT	20	6–14	Risperidone	0.7–1.5 mg/d, 0.03 ± 0.004 mg/kg/d	10	↓ CD
McCracken et al (2002)[78]	PDD + DBS	RCT	49	5–17	Risperidone	0.5–3.5 mg/d	8	↓ CD
Shea et al (2004)[77]	PDD + DBS	RCT	79	5–12	Risperidone	Mean 1.17 mg/d	8	↓ DBD
Snyder et al (2002)[74]	MR + DBS	RCT	110	5–12	Risperidone	0.02–0.06 mg/kg/d	6	↓ DBD
Van Bellinghen and De Troch (2001)[75]	MR + DBS	RCT	13	6–14	Risperidone	0.03–0.06 mg/kg/d	4	↓ CD
Neuroleptics								
Campbell et al (1984)[83]	CD	RCT	61	5–12	Haloperidol	1–6 mg/d	6	↓ CD symptoms
Greenhill et al (1985)[82]	CD	RCT	31	6–11	Molindone or thioridazine	Molindone mean 27mg/d Thioridazine mean 170 mg/d	4	Both drugs superior to placebo on aggression
Lithium								
Campbell et al (1995)[84]	CD	RCT	50	5–12	Lithium	Mean dose 1248 mg/d, mean serum level = 1.12 mEq/L	6	↓ CD symptoms
Campbell et al (1984)[83]	CD	RCT	61	9	Lithium	500–2000 mg/d, mean serum level = 0.99 mEq/L	6	↓ CD symptoms
Rifkin et al (1997)[129]	CD	RCT	33	12–17	Lithium	500–2000 mg/d	2	Lithium = placebo
Malone et al (2000)[86]	CD	RCT	40	12.5	Lithium	900–2100 mg/d, mean serum level = 1.07 mEq/L	6	↓ CD symptoms
Stimulants								
Klein et al (1997)[90]	CD + ADHD	RCT	84	12	Methylphenidate	20–60 mg/d	5	↓ conduct and ADHD symptoms
Hazell and Stuart (2003)[96]	CD/ODD + ADHD	RCT	38	6–14	Clonidine	Clonidine 0.10–0.20 mg/d added to stimulant	6	↓ conduct symptoms with combination

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, CD = conduct disorder, CO = crossover design, DBD = disruptive behavior disorder, DBS = disruptive behavior symptoms, MR = mental retardation, ODD = oppositional defiant disorder, PDD = pervasive developmental disorder, RCT = randomized, controlled trial.
Symbol: ↓ = decreased.

tive, suggesting caution in the use of this agent for aggression in this population.[88]

Stimulants

Maladaptive aggression is highly associated with ADHD. Controlled clinical research and 1 meta-analysis support the use of stimulants for aggression associated with ADHD[89,90] and possibly CD.[90,91]

Antidepressants

The effectiveness of antidepressants for treating aggression in children and adolescents with major depression has not been established.[3] No controlled studies to date have demonstrated that selective serotonin reuptake inhibitors are effective in reducing aggression in children and adolescents. One small, open-label study (N = 12) of citalopram 10 to 40 mg/day suggested effectiveness in

pediatric impulsive aggression.[92] These agents are especially interesting in the light of what we know about the role of serotonin in impulsive aggression.[93] Antidepressants such as bupropion[94] and tricyclic antidepressants such as desipramine[95] appear helpful in reducing aggression, but only when it occurs in the context of ADHD.

α-Adrenergic Agents

Clonidine is an α-adrenergic agonist that reduces norepinephrine outflow from the locus ceruleus. In the context of ADHD comorbid with conduct disorder and aggression, 2 controlled trials have demonstrated efficacy for aggression and conduct problems.[91,96]

Limitations of Psychopharmacologic Treatments of Aggression

Studies suggest that it is predominantly reactive, impulsive, affective aggression that responds to medication.[7,86,97,98] However, most studies do not separate reactive from proactive forms of aggression. This is an area of much-needed research. Instrumental/proactive types of aggression may have a limited response to pharmacologic treatments.

A number of issues have limited the development of psychiatric medications for aggressive children and adolescents. These issues include concerns about the multitude of psychosocial, community, economic, political, and family correlates of maladaptive youthful aggression and the likelihood that these issues, not narrowly defined neurobiological correlates of aggression, are in urgent need of national attention and resources. Medicating the chronically aggressive child or adolescent and missing the psychosocially relevant context in which aggression occurs is a persistent concern among clinicians as well as the lay public. Polypharmacy, or the use of multiple agents, often given in subtherapeutic doses for extended time periods without a clear definition of response or a clearly defined endpoint, is common in clinical practice and limits the endorsement of medications for aggressive behavior. The absence of a primary illness condition for the pharmaceutical industry to target and the reluctance to use target symptoms as a reason to develop medication treatment have limited both the development of medication treatments and the enthusiasm of the pharmaceutical industry for studying medications in youth with maladaptive aggression.

Without a consensus on how to define the types of aggression that might be the focus of different treatment approaches, it is unclear which aggressive child is likely to benefit from adjunctive medication treatment. No data exist from head-to-head comparisons of psychosocial versus medication approaches or integrated psychosocial and medication interventions versus either treatment alone in the treatment of aggression. Thus, we do not yet understand which aggressive child may benefit from medication. Some aggressive children become less aggressive with only increased environmental structure provided by an inpatient psychiatry unit, without the use of medication.[99] Because of the high responsiveness of some children's aggression to controlled and structured environments, future treatment studies should routinely report on these components in addition to the specific treatment being tested.

In summary, studies need to carefully define the type of aggression being treated in clinical trials and define aggression subtype, frequency, and severity as primary outcome measures. Presently, 2 meta-analyses of medication effects on overt aggression in psychiatrically referred children and adolescents with heterogeneous diagnoses find effect sizes that range from 0.44 to 3.0 for stimulants in ADHD; antipsychotics, mood stabilizers, and antidepressants in ADHD; and α-adrenergic agents in ADHD and serious emotional and behavioral disorders.[89,100]

SERVICE CONFIGURATION MODELS FOR AGGRESSIVE CHILDREN AND ADOLESCENTS

Empirically tested prevention models and treatment trials indicate the need for a long-term, comprehensive psychoeducational team approach to treatment for early-onset disorders of maladaptive aggression. The mental health care team and setting should include (1) a continuum of care ranging from ambulatory settings to highly structured inpatient crisis stabilization units, utilized for short periods of time when the child's aggression cannot be safely contained in less restrictive settings. (The setting in which treatment takes place is important. Individual interventions for maladaptive aggression may be ineffective unless provided in a milieu that can curtail dangerous behaviors); (2) therapists trained in psychosocial therapies known to be effective in changing mechanisms in families that promote aggressive and antisocial behaviors (e.g., PMT); (3) therapists trained in therapies that promote skill-building in children and their parents (conflict resolution strategies, social skill-building, CBTs); (4) parenting education and supports; (5) child and adolescent psychiatrists to complete a thorough evaluation of the child and family, assess for psychiatric disorders that might predict treatment response in the child, provide adjunctive psychopharmacologic treatments, effectively communicate with other team members about the child, and monitor outcomes; (6) psychoeducational evaluation to assess cognitive, language, and learning strengths and vulnerabilities and referral for special education remediation as needed; (7) a mechanism for regular multidisciplinary meetings to discuss progress concerning the child; and (8) resource support sufficient to deliver multidisci-

plinary psychoeducational services on a daily to weekly basis over an extended period of at least several years to the individual child or adolescent and his/her parents and family. Interventions with these characteristics are likely to reduce aggression in clinically referred children and adolescents. Treatments that are not comprehensive; are delivered in a fragmented, piecemeal fashion; and are short in duration appear doomed to failure in this population.

JUVENILE MALADAPTIVE AGGRESSION: QUESTIONS, FUTURE DIRECTIONS, AND A PROPOSED RESEARCH AGENDA

The identification, treatment, and prevention of excessive maladaptive aggression are important clinical and public health areas of focus for child and adolescent psychiatrists. Notably, the goal of treatment is not short-term reduction of aggression during the immediate treatment period but rather reduction in impulsive aggression across development. This goal will require studying aggressive children longitudinally for extended periods of time in different settings. Important questions and suggested avenues for future research directions are described in the following sections.

Developmental Psychopathology

Critical periods in development, during which empirically based interventions given for discrete durations might prevent a developmental trajectory into CD for at-risk children, need to be identified. Early-onset aggressors have a worse life-course prognosis than adolescent-onset aggressors.[101] Some evidence suggests that critical periods of development for diminishing aggressive behavior may be concentrated in the transitions from preschool to the elementary school years and from late adolescence to the young adult years.[30] Intensive treatment interventions focused during these times may alter the stability of aggression and yield large positive outcomes with regard to antisocial behaviors.

Mechanisms of Aggression

Research is needed to better identify biosocial interactive mechanisms in the etiology of pediatric disorders of aggression.[102] Distinctions between proactive and reactive aggression may facilitate such research, because their neuroarchitecture and neurocognitive mechanisms appear to be different.[67] The interaction between impulse dyscontrol and maladaptive rearing environments, as well as the interaction between developmental trauma and biological vulnerability in the etiology of aggression, are areas of important research. An example of this latter type of research are studies exploring the association between a functional polymorphism of the *MAOA* gene that appears to moderate the effects of maltreatment on aggression in males.[103] Once core interactive mechanisms in the genesis of maladaptive aggressive behavior have been identified, treatments can be designed to interrupt or diminish these specific processes in those at high risk.

Treatment of Maladaptive Aggression

Continued research is needed to identify important moderators and mediators of psychosocial treatment effects for aggression.

Research is needed to identify moderators and mediators of psychopharmacologic treatment effects for aggression.

Treatment research in the field would be advanced by direct comparisons assessing specific medications, specific psychosocial treatments, and their combination on measures of effectiveness, safety, and tolerability. These studies should include a determination of which type of aggressive children would benefit from which type of treatment.

Since many different systems of care are involved in the clinical treatment of aggressive children and adolescents, it is important to know more about how the various systems, including family, school, state agencies, protective services, and juvenile justice, influence treatment outcomes. There is a need for more information regarding optimal interdisciplinary interactions within as well as among various systems to maximize positive outcomes for these children and adolescents.

Psychopharmacology Questions

- Which medications targeted to treat which underlying psychiatric disorders will prove most effective in treating associated aggression?
- Is aggression better conceptualized on a continuum (as a dimensional variable) or as a discrete entity, such as the diagnosis of intermittent explosive disorder, for research purposes?
- What are the clinical parameters for psychopharmacologic intervention for childhood aggression?
- Which child is the optimal candidate for a medication intervention?
- What severity or chronicity criteria are needed before a clinical trial of medication is indicated?
- What types of medicines should be considered?
- What dose range and/or serum level should be considered in medication trials for disorders of aggression?
- When is combined pharmacotherapy with 2 or more agents warranted in the treatment of aggressive youth?
- What is a reasonable duration of medication treatment for maladaptive aggression?
- Given the intermittent nature of aggression for some children, how does the treating clinician define the end point of a medication trial?

Can a series of algorithms be developed to help standardize medication interventions in the different disorders with maladaptive aggression?

CONCLUSIONS

Therapeutic nihilism in the treatment of aggressive children and adolescents with conduct problems is no longer warranted. Multifocused psychosocial prevention interventions, especially given early in life to at-risk children and families, have the most support for efficacy. Emerging evidence suggests effectiveness for some psychopharmacologic agents in selected disorders. However, treatments for children and adolescents who routinely present with well-established disorders of aggression in the context of psychiatric diagnoses are neither robust nor well-established. Given the prevalence of aggression in clinically referred children and adolescents and the amount of health care resources consumed by disorders of aggression, the study of maladaptive aggression in clinical and juvenile justice settings needs to become a high priority.

Drug names: aripiprazole (Abilify), bupropion (Wellbutrin and others), carbamazepine (Carbatrol, Equetro, and others), citalopram (Celexa and others), clomipramine (Anafranil and others), clonidine (Catapres, Duraclon, and others), clozapine (Clozaril, FazaClo, and others), desipramine (Norpramin and others), divalproex sodium (Depakote), haloperidol (Haldol and others), lithium (Lithobid, Eskalith, and others), molindone (Moban), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon).

Financial disclosure: In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME article were asked to complete a statement regarding all relevant financial relationships between themselves or their spouse/partner and any commercial interest (i.e., a proprietary entity producing health care goods or services) occurring within at least 12 months prior to joining this activity. The CME Institute has resolved any conflicts of interest that were identified. The disclosures are as follows: Dr. Connor has received grant support from AstraZeneca and Cephalon; is a consultant to and has received honoraria from, and is on the speakers/advisory boards for Cephalon and Shire. Dr. Carlson has received grant/research support and honoraria from, and is a member of the speakers/advisory boards for Abbott, Janssen, Otsuka, and Eli Lilly. Dr. Chang is a consultant for AstraZeneca, Abbott, Eli Lilly, Shire, and GlaxoSmithKline; has received grant/research support from GlaxoSmithKline, Abbott, AstraZeneca, and Otsuka; and has received honoraria from AstraZeneca, Abbott, Eli Lilly, and GlaxoSmithKline. Dr. Findling has received grant/research support from Abbott, AstraZeneca, Bristol-Myers Squibb, Celltech-Medeva, Forest, GlaxoSmithKline, Johnson & Johnson, Eli Lilly, New River, Novartis, Otsuka, Pfizer, Shire, Solvay, and Wyeth; is a consultant for Abbott, AstraZeneca, Bristol-Myers Squibb, Celltech-Medeva, Forest, GlaxoSmithKline, Johnson & Johnson, Eli Lilly, New River, Novartis, Otsuka, Pfizer, Sanofi-Synthelabo, Shire, Solvay, and Wyeth; and is a member of the speakers bureau for Shire. Dr. Steiner is a speaker for Abbott, AstraZeneca, Janssen, and Eli Lilly; is an advisor/consultant for Abbott, Janssen, and Otsuka; has received unrestricted educational grants from Abbott, Janssen, Wyeth-Ayerst, Solvay, GlaxoSmithKline, McNeil-Alza, Novartis, Forest, and Pfizer; and has received research grants from Pfizer, Abbott, and Janssen; Drs. Daniolos, Ferziger, Hutchinson, Malone, Halperin, Plattner, Post, Reynolds, Rogers, and Saxena have no significant commercial relationships to disclose relative to the presentation.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, aripiprazole, bupropion, carbamazepine, citalopram, clomipramine, clonidine, clozapine, desipramine, divalproex sodium, haloperidol, lithium, molindone, olanzapine, quetiapine, risperidone, and ziprasidone are not approved by the U.S. Food and Drug Administration for the treatment of aggression and conduct disorder.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Childhood and Adolescent Mental Health section. Please contact Melissa P. DelBello, M.D., at delbelmp@email.uc.edu.

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