



Assessing and treating aggression in children and adolescents

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Abstract: Aggression is common in children and adolescents and has serious consequences. This manuscript reviews the following aspects of aggression: (I) types and causes, (II) components of a comprehensive assessment, (III) a comprehensive approach to treatment, (IV) recent evidence based psychotherapeutic treatments, (V) the recent evidence based psychopharmacological treatments and (VI) aggression outcomes. We conducted a selective review from the last two decades using terms, “aggression”, “children”, “adolescents” using PubMed and also PsychINFO for the psychotherapy literature, and PubMed alone for the psychopharmacology review. We also included additional relevant references. We provide evidence-based recommendations for the assessment and treatment of aggression for children and adolescents. Aggression treatment requires a comprehensive assessment, treatment for the underlying conditions and behavioral interventions/psychotherapy and may also include careful pharmacological treatment and eventual recovery and/or short/long-term monitoring. A comprehensive assessment includes gathering a thorough history, considering symptoms in a developmental context, interviewing the guardian and child separately and together, ruling in and out psychopathology and potential stressors, conducting a risk assessment and using rating scales at baseline to assist in diagnosis and to track symptoms. A comprehensive approach to treatment includes providing or assisting the family in obtaining evidence-based psychotherapy appropriate for the child’s age and developmental level, engaging the child, family and school in taking an active role in implementing psychosocial strategies and implementing the appropriate supports, following evidence-based guidelines to treat the primary (underlying) disorder with evidence-based psychotherapies and medications. The manuscript provides a review of the psychotherapeutic approaches that have been shown to be effective in treating aggression as well as the evidence for efficacy of the different classes of medication including psychostimulants, alpha agonists, antidepressants, atypical antipsychotics and mood stabilizers. Evidence supports that first line medication begins with optimization of pharmacological treatment for the primary diagnosis, for example the use of stimulants for children with attention deficit hyperactivity disorder (ADHD) and co-occurring aggression, followed by risperidone, and aripiprazole with substantial evidence supporting their effectiveness in treating aggression. Finally, we review the outcomes of aggression.

Keywords: Aggression; child and adolescent; review; psychotherapy; psychopharmacology

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Case presentation

Zoe¹, a 9-year-old girl, lives with her parents and two sisters (age seven and 14) and attends fourth grade where she receives resource room for math. During her annual well-child visit, her mother explains that she is concerned because for the past 6 months, Zoe has been having trouble with her behavior at home and school and that in the week before the visit, she became agitated when her mother tried to take away her iPad. She scratched and hit her mother, cracked the screen of the iPad, and destroyed her room. She presents today for a scheduled visit to clarify her mother's concerns.

Zoe has been more aggressive and stubborn since the middle of third grade. She spends hours each day using the family iPad to watch shows and play games. There have been times when her mother will take the iPad away but later find her watching videos late at night. When her parents try to set limits, she has a tantrum. During a tantrum, she yells, slams doors, throws toys, and has been physically out of control. She has yelled, "*I hate you,*" or "*I wish I was dead.*" She has been intolerant of her younger sister and has pushed and hit her. When she is not using screens, she complains that she is bored. Her mother describes her mood alternating between irritable and cheerful and does not think Zoe is worried, anxious, or sad on a daily basis. Teachers report that she can get frustrated at school if she perceives the work to be too difficult. She has crumpled her paper into a ball and run out of the classroom. She often needs one-on-one attention to complete her assignments. Her grades are approaching and meeting expectations, except for math which has always been challenging for her. When you meet with Zoe alone, she says her mood is "*okay.*" She denies any recent stressors including bullying or changes at home. She says her parents and her little sister are annoying and that it is not fair when her parents take the iPad away. She admits that at times she has trouble paying attention in school and that math is too hard. She denies any suicidal ideation. She denies any intent to harm others, but says that she hits her sister "*when she deserves it.*"

Zoe has never seen a therapist or psychiatrist before. She has an individualized education plan done in second grade due to some concerns with her learning. There is no evidence of trauma or substance use. Her developmental history is significant for some mild delays in reading. She has no significant medical history. She lives at home with her sisters and parents. She has been raised by her mother since she was

born and her father since he immigrated to the United States (US) when Zoe was two. She has friends from school and the neighborhood. She seems to be spending less time with them in person, but does play games with them on-line.

Zoe presents to her appointment wearing her school uniform. She has short pieces of hair in the front from cutting it herself a couple of months ago. Throughout the interview she has poor eye contact and is minimally cooperative. She shifts around on the examining table, tearing at the paper. She states her mood is "*okay*" but on further questioning she says that sometimes she is mad, sad or bored. When asked about the event that brought her in, she states that she does not want to talk about it. She denies any suicidal or intent to hurt others.

Introduction

Aggression affects 10–25 percent of youth (1) and is one of the most common reasons for referral to psychiatric care in children (2). It is a symptom that is common to many psychiatric disorders (3), is often stable and predicts social-emotional problems in adulthood (4). We will review (I) aggression in the context of development and the types of aggression, (II) components of a comprehensive assessment, (III) components of a comprehensive treatment, (IV) evidence-based psychotherapeutic treatments, (V) evidence-based psychopharmacologic treatments, and (VI) outcomes of aggression.

Methods

For this selective review, we conducted a search on MEDLINE from 2000 to 2020 using the search terms "aggression", "children" and "adolescents". For the psychotherapy section, we also searched PsychINFO. We additionally included relevant articles drawn from bibliographies of the articles we identified in searches. This manuscript did not require IRB approval.

Aggression and development

Learning how to best regulate aggression is a normal part of child development. Typically, physical aggression peaks at 18–24 months and decreases by age five as children learn to self-regulate their emotions and impulses (5). As children develop verbal skills, they begin to communicate their

¹Zoe is fictional case who represents a common presentation of aggression in a child.

thoughts and feelings and display verbal forms of aggressive behavior (6). During the early school-age years (ages 4 to 7), as children begin to have greater interaction with their peers and form relationships, indirect aggression (e.g., relational and social) begins to increase, especially for girls (7). This is due in part to children's increase in cognitive and social skills and their ability to recognize that this form of aggression is less detectable, hence less punishable (8). As children enter their adolescent years, they become more aware of their self-identity and social standing with their peers. The desire to fit in and gain popularity can lead to an increase in aggression, sometimes in the form of violence, to other children and authority figures (9). In differentiating normal aggression from pathological aggression, it is important to note the intensity, frequency, impairment and course. Aggression that persists through the first 5 years of age is considered abnormal (10). Unlike normal aggression which is transient, pathological aggression continues to cause dysfunction, often times with greater frequency and intensity over time (11).

Types and causes of aggression

Aggression can have various etiologies including genetics, environment, development and pathology and can be adaptive or maladaptive. Adaptive aggression is a normal part of development, arises from the central nervous system and serves pro-social aims, including resource acquisition, defense of the individual or group and establishment of dominance in social groups (12). There are many ways to characterize maladaptive aggression; it is often broadly classified as impulsive versus predatory. Impulsive aggression tends to be unplanned and uncontrollable, whereas predatory aggression involves calculated, self-serving efforts (13). In a recent review, Connor and colleagues classified aggression into more specific subtypes to further differentiate behavioral patterns including reactive, impulsive and affective aggression versus predatory or proactive aggression. Reactive aggression usually manifests as hostile, labile behavior as a response to frustration, whereas proactive aggression is intentional and goal-directed (12). Finally, another useful way of conceptualizing aggression is to categorize it into the following subdivisions: impulsive, predatory, affective storm, anxious/hyperarousal, and cognitive/disorganized (14). These categories and framework are addressed in *Table 1* and are especially useful as they are associated with hypothesized biological mechanisms and diagnoses [(14), Kaye DL 2020, personal

communication, December 14, 2020].

When evaluating a patient presenting with aggression, it is important to consider their developmental level as well as the type of aggression. Zoe's aggression is impairing, and beyond what one would expect for her developmental age. Zoe, above, appears to be presenting with reactive or impulsive aggression. Aggression can be a symptom of various child psychiatric disorders and the type of aggression can give us some clues to the causes. In Zoe's case, the doctor is considering attention deficit hyperactivity disorder (ADHD) or a mood disorder, major depressive disorder or persistent depressive disorder. The next step to providing Zoe with comprehensive care is to conduct a comprehensive assessment, described in the next section.

Comprehensive assessment

Aggression in children and adolescents can be the result of a multitude of factors. Therefore, when a child or adolescent presents with aggressive behavior, the first step is to conduct a comprehensive assessment. Components of this assessment include: (I) building a therapeutic alliance, (II) gathering a thorough history, (III) interviewing the parent or guardian and the child separately, (IV) ruling in and out relevant psychopathology, (V) conducting a risk assessment and (VI) tracking symptoms from baseline with rating scales (13).

Therapeutic alliance

A comprehensive assessment is best facilitated when the healthcare provider builds a strong alliance with the child and their parents. Various studies highlight the importance of establishing a solid alliance and its impact on improving outcomes (15,16). Components of a strong alliance can include: understanding the patient and parent priorities, cultural competence and provider characteristics such as increased interpersonal warmth (17). Over time, the strength of this therapeutic alliance must be reevaluated to ensure effective treatment.

Gathering a thorough history

The second step in conducting a comprehensive assessment is to gather a thorough history from the parents or guardians, child, teachers (with permission), and other pertinent individuals. This initial evaluation elicits details regarding the presenting concern and symptoms, past history of behavioral symptoms, psychiatric history and review of symptoms,

Table 1 Types of aggression and commonly associated diagnoses (Kaye DL 2020, Personal Communication, December 14, 2020) (14)

Aggression type	Description	Associated diagnoses
Impulsive	Unplanned, unprovoked, uncontrollable, hasty, unable to perceive repercussions/delay gratification; excessive, unexpected	ADHD Bipolar disorder Intermittent explosive disorder Traumatic brain injury
Predatory	Calculated, self-serving motivation, aware of harm caused by actions; premeditated	Autism spectrum disorder Conduct disorder
Affective storm	Out-of-proportion response to provocation; reactive, dysregulated mood, unable to regulate arousal; usually extended in duration (>30 minutes)	ADHD Autism spectrum disorder Bipolar disorder Disruptive mood dysregulation disorder Intellectual disability Major depressive disorder/persistent depressive disorder Substance abuse disorder
Anxious/hyperarousal	Overwhelmed response to anxiety; anxiety may cause irritability and over-reaction, relief of tension follows aggressive act	Anxiety disorders (generalized anxiety) Autism spectrum disorder Obsessive compulsive disorder Post-traumatic stress disorder
Cognitive/disorganized	Skewed perceptions, delusions, paranoia, abnormal reasoning	Bipolar disorder Psychosis Schizophrenia Substance abuse Traumatic brain injury/fetal alcohol syndrome/brain damage

ADHD, attention deficit hyperactivity disorder.

developmental history, medical history, previous trauma and abuse, substance use history and family history. For the presenting concern, it is important to seek a thorough understanding of the symptoms and their precipitants. Gathering information on parenting methods and details regarding home and school environment are critical in further evaluating the context of the patient's behavior. Understanding the child's school history and functioning are especially important because the need for further academic support or a different setting may be contributing to the child's behavioral dyscontrol. It is also important to consider symptoms in a developmental context. For example, up till age five, physical aggression that is transient and mild in nature is considered normal. As children age, normative

aggression becomes less frequent. When aggression persists, or onsets at an older age, it may be cause for concern.

For Zoe, it was unclear what may have led to her worsening aggression, but there were some clues. For her, limit setting played a role, especially taking away her iPad. It appeared that she had become increasingly moody at home and school. Her doctor wisely questioned her about problems with friends, bullying and abuse, all of which she denied. Another possible contributor was her performance in school and her learning difficulties were contributing to her increased frustration. Thus, for Zoe, her doctor spoke with her mother about bringing in report cards and asking the teachers to complete some rating scales. Considering Zoe's developmental stage, by age nine, she should have

developed sufficient social skills to be able to communicate her feelings and desires without resorting to physical aggression. Her tantrums that include yelling, slamming doors, and throwing toys—which can be considered normal during the first 3 years of life—are atypical at her age.

Interviewing the parent or guardian and the child separately

It is important to interview the parent and child separately if possible and to also see how they interact together. Parents may feel more comfortable sharing their concerns with their children out of earshot. Similarly, children and adolescents may be more able to engage and share sensitive information such as trauma without their guardian present. During this part of the evaluation, the clinician can gather information on the child's appearance, speech, affect, mood, thought process, cognitive processes insight, judgment and risk status (described more below) for the mental status exam. Additionally, observing the parent-child interaction can also give clues to how they relate at home, and may be helpful in developing effective interventions.

Ruling in and out psychopathology and potential stressors

When a child presents with aggression, it is important to carefully rule in and rule out psychiatric causes and comorbidities such as ADHD, anxiety disorders, mood disorders, intellectual disabilities, and substance abuse disorder as the cause or contributor to the patient's symptoms. Making note of risk factors such as community violence, peer pressure, and access to weapons can better inform health care providers in the process of making a customized treatment plan. *Table 1* includes different psychiatric diagnoses that may be associated with aggression.

For Zoe, gathering a more detailed history from Zoe, her mother and later, from her teachers, led to the conclusion that she had previously undiagnosed ADHD and that her trouble with attention was leading to challenges at school. In addition to more frequent outbursts at home, she was also more irritable. Here it was unclear if the irritability was consistent with mild depression or disruptive mood dysregulation disorder (DMDD). Her doctor decided to first prioritize treating her ADHD and to monitor the irritability and aggression.

Conduct a risk assessment

Performing a risk assessment of the patient is a critical

portion of the comprehensive assessment. Ensuring a patient's safety is crucial prior and during the implementation of a treatment plan. A risk assessment includes the identification, analysis, evaluation, and treatment of risks (18). In considering the patient's psychological factors (e.g., their current mental health), social factors (e.g., home and school environment, family dynamics), vulnerability, previous history of self-harm, violence, and abuse, and access to substances and weapons, a risk assessment can determine their care needs and evaluate their risk of harm to themselves and others. This allows healthcare providers to work more efficiently with the patient's family and guardians to promote their safety and wellbeing (19). Particular attention should be given to the child's access to firearms and other weapons as they are particularly concerning for harm to self, to others, and for impulsive acts of aggression. Analysis of risk involves considering the conditions that can increase and decrease risk such as substance use, personality, and protective factors. Evaluation of risk involves assessing severity, duration, and nature, and it provides information that can be used to develop an appropriate treatment plan to promote the safety of the child and the family.

Use rating scales to track symptoms

Rating scales can be very helpful in assessing aggression at baseline and monitoring progress with treatment. Rating scales for, e.g., ADHD, anxiety and depression can also be useful in helping to rule in and rule out other coexisting conditions that may contribute to the aggression. Aggression scales such as the Modified Overt Aggression Scale (MOAS) (20), Outburst Monitoring Scale (OMS) (21), the Impulsive/Premeditated Aggression Scale (IPAS) (22), the Children's Aggression Scale-Parent and -Teacher versions (CAS) (23,24), and Children's Inventory of Anger (ChIA) (25) can help describe and quantify symptoms to establish a starting point for the child's behavior.

Comprehensive approach to treatment

Developing a treatment plan for youth with aggression begins with comprehensive assessment. As described above, this evaluation should ideally involve obtaining collateral information from daycare and school teachers and other adult figures in the child's life as they may also be instrumental as part of the treatment plan (13). The treatment plan should meet the individual needs of the

child based on their age, developmental level, diagnosis, and psychosocial context. Given the causes of aggression are often multifactorial, the approach to treatment can be complex and address multiple environmental and psychiatric causes. The Center for Education and Research on Mental Health Therapeutics (CERT) Guidelines for the Treatment of Maladaptive Aggression (TMAY) II (26) effectively addresses these components in their consensus paper with eleven guidelines. We have adapted and expanded upon the first five recommendations below.

- (I) Provide or assist the family in obtaining evidence-based psychotherapy;
- (II) Engage the child, family and school in taking an active role in implementing psychosocial strategies and implementing the appropriate supports;
- (III) Initiate psychopharmacologic treatment to treat the underlying psychiatric conditions;
- (IV) Follow evidence-based guidelines to treat the primary (underlying) disorder;
- (V) If residual aggression persists after steps 1 to 4, consider adding an atypical antipsychotic.

The remaining CERT guidelines address details on the safe prescribing of atypical antipsychotics, which is beyond the scope of this paper. In the following two sections, we review the most up to date psychotherapeutic and psychopharmacological interventions for aggression.

For our case example, Zoe, her doctor first addressed treatment of her primary condition, ADHD, with stimulants. Additionally, her doctor referred Zoe and her mother to a local therapist, who worked with Zoe's mother on parent management training. This combination led to significant improvements in Zoe's behavior so at that time, further psychopharmacological treatment targeting Zoe's aggression was not needed.

Below, we address the evidence base on psychotherapeutic and psychopharmacologic interventions for the treatment of aggression.

Follow evidence-based guidelines to treat the primary (underlying) disorder

As noted above, aggression is a symptom that can co-occur with many psychiatric disorders and in the setting of psychosocial stressors. Thus, we recommend taking an evidence-based approach to addressing those conditions and concerns as a first step when approaching treatment for aggression. For example, if a child's ADHD is effectively treated, they may be less impulsive and thus less aggressive. Or if they are no longer depressed, they may be less irritable and less likely to lash out violently at home.

Effective treatment of these conditions may lead to decreased aggression in some cases. However, there are often cases when a targeted treatment for aggression is needed.

Psychotherapy for aggression

Researchers have developed and evaluated multiple psychotherapeutic approaches to treating aggression in children and adolescents and have demonstrated them to be effective. Most of these treatments are guided by the social learning theory and developmental principles, varying based on the age of the child. For younger children, effective programs typically include behavior modification and an emphasis on helping parents improve parent-child interactions. For adolescents, many programs work closely with the adolescent themselves, incorporating cognitive behavioral principles to address their maladaptive behavior. They may also work with parents/caregivers to assist in setting limits and encouraging pro-social behaviors. Treatments that have been shown to be effective vary in the setting (outpatient, home-based, school-based) and whether they are delivered individually or a group format. Additionally, the various well-researched evidence-based therapies can be categorized generally as parent-centered, child-centered, family-centered, and multi-component. We will describe some of the therapies with the greatest evidence for efficacy below.

Parent-centered programs (preschool and school aged)

For children ages 12 and younger, there are multiple evidence-based therapies that have been shown to be effective. Many of these focus on working with parents to improve parenting skills and enhance the relationship between the parent and child through effective emotional communication. Many parent focused treatments are considered "parent management training" and can be done in an individual or group format. Therapists teach parents such as having consistent quality time, positive reinforcement of desired behaviors and other behavior management techniques. Some of the most well-studied intervention programs with evidence for efficacy in treating aggression include the Chicago Parenting Program (CPP) (27), Parent-Child Interaction Therapy (PCIT) (28), Helping the Non-Compliant Child Program (NCCP) (29), the Parent Management Training-Oregon model (PMT-O) (30), and the Triple P Positive Parenting Program (31). *Table 2* provides a description of psychotherapies with evidence for efficacy based on controlled trials.

Table 2 Psychotherapy for the treatment of aggression

Intervention	Ages	Description	Studies showing efficacy
Parent-centered programs			
Parent-Child Interaction Therapy (PCIT)	2–7 years	Dyadic intervention: parents learn how to improve quality of parent-child interactions through play and effective discipline techniques Sessions held both solely with parents and also with the child as the therapist coaches parent via a “bug in the ear”	Meta-analysis of 24 studies demonstrated PCIT associated with reduced parent-reported externalizing behavior in children (28) Improvement maintained as far as six years post-treatment (32)
The Chicago Parent Program (CPP)	2–5 years	Prevention intervention, 12 group sessions and video vignettes to stimulate discussion and problem solving related to child behavior and parenting skills; designed to engage low income African American and Latino families Focuses on building parents’ positive relationships with children, behavior management, stress management, problem-solving and skill maintenance (27)	Effective in multiple studies including in comparison to PCIT in a pragmatic, non-inferiority trial (27)
Helping the Non-Compliant Child Program (NCCP)	3–8 years	8–10 1-hour long group sessions Teaches parents to promote prosocial interactions and intentionally ignore their child when engaging in maladaptive behaviors (29)	Effective in reducing disruptive behavior and improving parenting skills (33)
Parent Management Training-Oregon (PMT-O)	2–18 years	20 sessions Sharpening parenting skill and refraining from using coercive methods, skills include limit setting, reinforcing prosocial behavior, monitoring and supervision, regulating emotion and interpersonal problem solving	RCTs evaluating the PMT-O model in children ages 4–12: superior to alternative treatments in reducing aggression (30,34,35) even up to 2 years post-treatment (36)
Triple P Positive Parenting Program	<16 years	Multi-tiered program that adjusts treatment intensity according to the severity of the child’s disruptive behavior Parents gain knowledge and skills through various modalities such as group and individual sessions according to specific needs	RCT: Triple P reduced maladaptive behavior in children and improved parenting skills for children with ADHD and co-occurring disruptive behavior disorders (37) Meta-analysis of 55 studies: Triple P associated with positive changes in child behavioral problems and parenting skills (31)
Child-centered programs			
Anger Coping Program	8–14 years	18 1-hour long sessions, incorporate didactic explanations, group discussions, role plays and games Based on cognitive behavioral therapy and designed to be implemented in small groups in schools Children learn to decrease disruptive behavior towards authority figures and increase self-esteem (40) Coping Power Program: modification that includes child and parent component, 33 group sessions involving role-playing, therapist modeling and homework (38,39)	RCTs: decreases parent and teacher-reported aggression and delinquency (38,39)

Table 2 (continued)

Table 2 (continued)

Intervention	Ages	Description	Studies showing efficacy
Problem-Solving Skills Training Program	7–14 years	12-week program, children's aggressive behavior attributed to deficits in interpreting others' intentions Therapist assists child in viewing their relationships in a positive manner through techniques such as reinforcement, role playing, and feedback (42)	RCTs: associations with less aggressive behavior and delinquency, and more prosocial behavior (41)
Family-centered programs			
Functional Family Therapy (FFT)	11–18 years	8–12 1-hour sessions, resolving conflict and improving communication between family members Treatment phases include engagement and trust building, addressing behavioral change in familial relationships, and generalization After building alliance and motivation, therapist evaluates familial interactions in order to promote prosocial behavior through techniques such as cognitive reframing and attentive listening (43)	FFT superior to alternative treatments conditions for delinquent children (43)
Brief Strategic Family Therapy (BSFT)	6–18 years	4 months of weekly sessions Based on the strategic family theories, addresses negative familial interactions that sustain a child's disruptive behavior, focus system, structure of interactions, and strategy (44)	Improved family engagement and functioning and reduced anger, aggression, conduct problems, and substance use in children (44)
Collaborative and Proactive Solutions (CPS)	4–14 years	12 sessions attended by child and caregiver, developed for oppositional and explosive children (45) Identification of lagging skills and unsolved problems, discuss how parents' responses can reinforce problem behaviors, prioritization and teaching the family about the problem-solving framework Based on Greene's CPS model (47,48)	Randomized controlled comparative efficacy trial as well as other RCTS, CPS was shown to improve aggressive behavior (45,46)
Multimodal programs			
Multisystemic Therapy (MST)	12–17 years	Family-based treatment, based on social ecological perspective, evaluates various individual, peer, family, and community factors associated with aggressive behavior (49) Therapists formulate a customized treatment plan, includes techniques and strategies from various, well-studied cognitive-behavioral and family therapies Delivered in home setting with team of trained therapists who are available 24/7 and meet with child, family, school, etc. (49)	RCTs demonstrated efficacy in reducing aggressive behavior in adolescents, especially those involved in the justice system (50) Disruptive children recruited from behavior intervention classrooms who were not justice-involved showed greater improvements in comparison to services as usual persisting at 18-month follow-up (50)

Table 2 (continued)

Table 2 (continued)

Intervention	Ages	Description	Studies showing efficacy
Treatment Foster Care Oregon	3–17 years	Places adolescents with severe disruptive behavior in foster care with trained foster parents, eventually transitioning them back to original home after treatment Derived from social learning theory, incorporates cognitive and behavioral techniques implemented within a social ecological context (53) Trained foster parents promote prosocial interactions and satisfactory school performance, while discouraging engagement with troublesome peers. Practices reviewed in individual therapy, mentorship meetings and skills-building classes, point system to track progress Adolescent's family undergoes parenting training on discipline, problem-solving strategies, and management of their disruptive child (53)	Studies have shown that efficacy in reducing aggressive behavior (51,52)

ADHD, attention deficit hyperactivity disorder.

Child-centered programs

Child-centered programs use elements of cognitive behavioral therapy and focus on assisting the child in recognizing triggers associated with their aggressive behavior, challenging their cognitive perceptions, and improving problem-solving techniques. Two evidence-based examples of child-centered programs include the Anger Coping Program (40) and the Problem-Solving Skills Training program (41).

Family-centered programs

Family-centered programs focus on addressing dysfunctional interactions between family members in order to reduce aggression in children. In multiple sessions, families improve communication by learning prosocial skills such as cognitive reframing and attentive listening. Additionally, with a therapist's guidance, they address unresolved conflicts and negative habits that perpetuate the child's aggressive behavior. Three of the most well-studied family centered therapies include the Functional Family Therapy (FFT) (43), the Brief Strategic Family Therapy (BSFT) (44), and the Collaborative Proactive Solutions (CPS) (45).

Multimodal psychotherapies

Multimodal therapies are treatment approaches that combine different methods of interventions to better

customize a treatment plan that suits the needs of the child. They are typically used in more severely affected children and adolescents. These therapies implement a more complex and comprehensive approach to address the various factors that contribute to a child's maladaptive behavior. Some programs involve additional parties, such as the school and judicial systems, to create a more customized treatment strategy for the child. Two of the most studied evidence-based treatments include Multisystemic Therapy (49) and Treatment Foster Care Oregon (53).

Psychotherapy summary

There are many psychotherapeutic approaches with good evidence for efficacy for the treatment of aggression and thus behavioral interventions are a critical component of treatment. The specific type of intervention will vary based on factors such the child's age, developmental stage, the setting and the resources of the community. It is important to incorporate these therapies as part of the treatment plan.

Psychopharmacology

As described above, prior to considering the use of medication to target aggression, we recommend a comprehensive assessment, treating the primary disorder using evidence-based guidelines (and this may include both psychotherapeutic and psychopharmacological treatments), using psychosocial interventions, and taking

into account the child's age and development. For example, when considering treatment of the primary disorder, many studies have demonstrated that in children with ADHD, medications used to target ADHD also decrease aggressive behavior. When a child or adolescent has severe and impairing aggression after adequate trials of psychotherapy and medication for the primary disorder, a prescribing clinician should consider addition of medication. When considering medication for very young (pre-school aged) children, further caution is required and the process of diagnosis and assessment and is more elaborate in comparison with older children. Gleason and colleagues (54) developed algorithms, all beginning with a careful diagnostic assessment that considers developmental stage, and symptomatic variability. Treatment recommendations nonpharmacological interventions preceding pharmacological ones. In this section below, we review the recent evidence on the efficacy for treating aggression for the following drug classes: stimulants, alpha agonists, atomoxetine, selective serotonin reuptake inhibitors (SSRIs), atypical antipsychotics and mood stabilizers.

Stimulants

In the past two decades, multiple studies have demonstrated the efficacy of stimulants in reducing aggression in children with ADHD and disruptive behavior disorders. Among children and adolescents with a primary diagnosis of ADHD, investigators have found that stimulants effectively reduce aggression. Sinzig and colleagues (55) performed a double-blind, randomized trial comparing long-acting methylphenidate (MPH) to placebo to assess improvements in severe aggression and oppositional defiant disorder/conduct disorder (ODD/CD) symptoms in children with ADHD and found that MPH improved oppositional behavior and physical aggression in school and home, with greater improvements observed at school. Connor and colleagues (56) conducted a meta-analysis of randomized controlled trials (RCTs) examining the use of stimulants to treat children with ADHD and aggression and found that stimulants effectively decreased aggression, with a greater effect for overt aggression compared to covert aggression. Pringsheim and colleagues (57) compared the effectiveness of psychostimulants with other agents in treating children with ADHD and co-occurring ODD/CD and found that psychostimulants were most effective with an effect size (ES) of 0.84. Older trials have shown that MPH is effective in treating aggression in children with CD, both with (58) and

without (59) co-occurring ADHD. Similarly, Pappadopulos and colleagues (60) found that in comparison with other drug classes, stimulants effectively reduced aggression in youth with varied primary diagnoses of ADHD, autism spectrum disorder (ASD), mental retardation, and disruptive behavior disorders with or without comorbid diagnoses of CD, ODD and ADHD (ES =0.78). They also found that MPH was especially effective in treating youth with ADHD and aggression, with an ES of 0.9. Further supporting this, the Canadian Guidelines on Pharmacotherapy for Disruptive and Aggressive Behaviour in Children and Adolescents with Attention-Deficit Hyperactivity Disorder, ODD or CD recommend stimulants for youth with ADHD and aggression based on the strong pharmacological evidence (61). Taken together, these studies indicate that there is a great deal of evidence that supports the efficacy of stimulants in treating aggression, especially but not exclusively in child and adolescent patients with ADHD.

Alpha agonists

There is a small body of evidence to support the use of alpha 2 agonists to treat aggression, or related oppositional and conduct symptoms in children with ADHD. Connor and colleagues (62) examined the use of clonidine versus MPH versus the combination to treat oppositional symptoms in children with ADHD and aggressive ODD or CD and showed that all three treatments led to improvement in ADHD, CD and ODD symptom severity. In a later study, Connor and colleagues (63) examined the use of extended release guanfacine for children with ADHD and oppositional symptoms and found a decrease in oppositional symptoms in the guanfacine group through post-hoc analysis. The authors did not report specifically on aggression in either study. Hazell and colleagues (64) conducted an RCT of clonidine as an adjunctive treatment to psychostimulants for children and adolescents with ADHD with comorbid ODD or CD. They found a greater percentage of improvement in aggression in those treated with Clonidine than Placebo. Pringsheim and colleagues (57) reported a higher ES (0.43) for guanfacine than clonidine (ES =0.27), although both agents had lower ES than stimulants, as noted above.

Atomoxetine

Atomoxetine has not been shown to be effective in treating pediatric aggression. In a meta-analysis Pringsheim and

colleagues compared the effectiveness of atomoxetine to psychostimulants and found that it had a low ES (0.33) when managing oppositional behavior, conduct problems and aggression in children with ADHD. Similarly, in their review, Pappadopulos and colleagues (60) found an overall ES of 0.18 in the treatment of aggression in youth with a primary diagnosis of ADHD and co-occurring disorders. There are controlled studies that have shown atomoxetine's effect in improving ADHD symptoms, none of them comment specifically on aggression treatment (65,66).

SSRIs

In one recent study, investigators examined the treatment of irritability for children with the research diagnosis of severe mood dysregulation (SMD) comparing citalopram to placebo when added to MPH monotherapy and found that it reduced severe irritability in children and adolescents unresponsive to MPH alone (67). While the study was designed to examine the treatment of SMD, post hoc analyses showed that 98% of the participants also met criteria for DMDD. Their study did not specifically address aggression. An open trial by Armenteros and colleagues demonstrated citalopram was effective in treating impulsive aggression in children and adolescents with varied primary psychiatric diagnoses (68).

Atypical antipsychotics

Investigators have studied second generation antipsychotics for treating aggression and examined the use of atypicals for the treatment of aggression associated with diverse diagnoses. Please see *Table 3* for the RCTs of atypical antipsychotics for the treatment of aggression and related conditions from 2000 to 2020. The medication with the most evidence for efficacy is risperidone and is often considered the first line psychopharmacological treatment for residual aggression. Risperidone's efficacy in treatment is well-established in the treatment of irritability associated with ASD, and aggression in children with CD and ADHD (72,73,75).

Several studies have demonstrated aripiprazole's efficacy in treating irritability, although not aggression specifically, for children and adolescents who have ASD (82,83) and one demonstrated that aripiprazole decreased aggression in bipolar disorder (88). Both aripiprazole and risperidone have a US Food and Drug Administration (FDA) indications for the treatment of irritability associated

with ASD but are prescribed off label for aggression. In the US, there are no medications with an FDA indication for aggression. In Europe, there's an indication for short-term treatment (6 weeks) with risperidone for aggression in children age 5 and above and adolescents with subaverage intellectual functioning or mental retardation (105).

Evidence supporting the use of other atypicals for aggression is limited. Two studies have examined the efficacy of olanzapine in treating aggression and with mixed results (90,92). One RCT examined the use of clozapine versus risperidone in the treatment of aggression in children with CD and found both to be effective (93). Quetiapine, ziprasidone and lurasidone have minimal evidence supporting their use (97,102,104). Taken together, the strongest evidence is for the use of risperidone.

As with any treatment, it is important to also consider when and if to discontinue the use of atypicals. Studies have demonstrated the benefits of continuing risperidone for short-term maintenance therapy of four months after the acute stabilization phase to prevent the return of aggression (106,107) Guidelines such as the Treatment Recommendations for the Use of Antipsychotics for Aggressive Youth (TRAAY) emphasise the consideration of tapering the atypical antipsychotics after a 6- to 9-month period without aggression given the risk benefit of therapeutic and adverse effects (108).

Typical antipsychotics

We do not recommend typical/first generation antipsychotics as a first line treatment due to risk of long-term side effects such as tardive dyskinesia. Several early studies and more recent research on a new agent support their efficacy. Campbell and colleagues (109) conducted a double blind trial comparing haloperidol, lithium and placebo for treatment-resistant hospitalized children with CD aggressive type and found that both haloperidol and lithium were superior to placebo in decreasing behavioral symptoms, but that haloperidol was associated more often with adverse effects. In an older double-blind parallel group study, Greenhill and colleagues (110) demonstrated that molindone was as effective as thioridazine in reducing aggression in children hospitalized with under socialized CD, aggressive type. A newer formulation of extended-release molindone, SPN-810, is in development for treating children with ADHD and persistent impulsive aggression (111). In a double-blind placebo-controlled trial, SPN-810 was added to existing ADHD monotherapy and

Table 3 Randomized controlled trials of antipsychotics for the treatment of aggression and related conditions from 2000 to 2020*

Author year	Primary diagnosis	Study type	Age	Results
Risperidone				
Armenteros 2007, (69)	ADHD + aggression	Placebo controlled augmentation study	7–12 years	RISP > PBO modestly effective when used in combination with psychostimulants for treatment-resistant aggression
Gadow 2014 (TOSCA), (70)	ADHD + comorbid CD/ODD w/severe aggression	DBPCT augmentation study	6–12 years	RISP > PBO for aggression & ODD symptoms for patients receiving stimulants and behavior therapy
Blader 2021, (71)	ADHD + aggressive behavior	DBPCT augmentation study	6–12 years	RISP > PBO greater reductions in aggression
McCracken 2002, (72)	ASD	Multisite, randomized, double-blind trial	5–17 years	RISP effective and well tolerated for the treatment of tantrums, aggression, or self-injurious behavior
Shea 2004, (73)	ASD and other PDDs	Randomized, double-blind, placebo-controlled	5–12 years	RISP > PBO mean decrease on the irritability subscale of ABC
Research Units on Pediatric Psychopharmacology Autism Network 2005, (74)	ASD	Blinded discontinuation trial	5–17 years	Disruptive and aggressive behavior returned rapidly after discontinuing RISP
Levine 2016, (75)	ASD + irritability	Multisite, randomized, double-blind	5–17 years	RISP strong effect on symptom change (irritability decrease: ES =1.9, NNT =2)
Findling 2000, (76)	CD	DBPCT	6–14 years	RISP > PBO in ameliorating aggression on most measures
Buitelaar 2001, (77)	DSM-IV disruptive behavior disorders + subaverage intelligence	Double blind randomized parallel group	Mean age 14 years	RISP > PBO Improvements CGI-S, MOAS, ABC
Aman 2000, (78)	Subaverage IQ	Randomized double-blind	5–12 years	Risperidone effectively reduced disruptive behaviors
Aman 2002, (79)	Subaverage IQ	DBPCT	5–12 years	Risperidone effective and well tolerated for the treatment of severely disruptive behaviors
Van Bellinghen 2001, (80)	Low IQ	Double-blind, placebo-controlled	6–14 years	short-term, well tolerated, RISP > PBO in controlling behavioral disturbances in children with low IQ.
Snyder 2002, (81)	Subaverage IQ + severely disruptive behavior (80% w/ ADHD)	DBPCT	5–12 years	Risperidone effectively reduced aggression and disruptive behavior
Aripiprazole				
Marcus 2009, (82)	ASD + irritability	DBPCT	6–17 years	Significant reduction in irritability with all three fixed doses of Aripiprazole using the Aberrant Behavior Check-list-Irritability (ABC-I) subscale and Clinical Global Impressions-Improvement scale (CGI-I)

Table 3 (continued)

Table 3 (continued)

Author year	Primary diagnosis	Study type	Age	Results
Owen 2009, (83)	ASD + irritability	DBPCT	6–17 years	ARIP > PBO mean improvement ABC-I and CGI-I score week 1 through week 8
Findling 2014, (84)	ASD + irritability	DBPCT	6–17 years	No significant difference between ARIP and PBO in time to relapse during maintenance therapy
Ghanizadeh 2014, (85)	ASD	Randomized double-blind clinical trial	4–18 years	ARIP and RISP lowered ABC scores during 2 months
Fung 2016, (86)	ASD + impulsive aggression	Metanalysis	2–17 years	RISP and ARIP treatment of irritability of 0.9 and 0.8 respectively
DeVane 2019, (87)	ASD	Randomized double-blind parallel group	6–17 years	Aggression improved with both significantly with youth taking RISP and ARIP, RISP > ARIP group at weeks 3
Mankoski 2011, (88)	BD	DBPCT	10–17 years	Statistically significant improvement in irritability, aggressive behavior and motor activity/energy using the Young Mania Rating Scale
Olanzapine				
Hollander 2003, (89)	ASD	Open trial	6–14 years	Olanzapine showed reduced irritability and global improvement of ASD symptoms
Hollander 2006, (90)	PDD	RCT	6–14 years	General improvement in autism symptoms without specific anti-aggressive effects
Masi 2006, (91)	CD	Retrospective chart review	11–17 years	60% of patients responders, reductions in score on MOAS, CGI-I, CGAS
Stephens 2004, (92)	Tourette's syndrome	RCT	7–13 years old	Olanzapine effective in reducing aggression and tics
Clozapine				
Juárez-Treviño 2019, (93)	CD	RCT	6–16 years	Clozapine and RISP effective for short-term treatment of aggression
Kranzler 2005, (94)	Treatment refractory schizophrenia	Open trial	8.5–18 years	Clozapine decreased aggression and enabled discharge
Quetiapine				
Findling 2006, (95)	ADHD + CD + aggression	Open label trial	6–12 years	Baseline score of the RAAPPS, and several subscales of the NCBRF and the CPRS decreased by the end of the study
Kronenberger 2007, (21)	ADHD + CD/ODD + aggression	Augmented open label trial	12–16 years	Adding Quetiapine to OROS MPH effectively reduced ADHD and aggression, in partial responders
Golubchik 2011, (96)	ASD + aggression	Open label trial	13–17 years	Quetiapine significantly reduced severity of aggressive behavior

Table 3 (continued)

Table 3 (continued)

Author year	Primary diagnosis	Study type	Age	Results
Barzman, 2006, (97)	BD and disruptive behavior disorders (ODD or CD)	DBRCT	12–18 years	Quetiapine and divalproex similar efficacy for treating impulsivity and reactive aggression
Masi 2015, (98)	BD + CD	Open-label, flexible-dose comparative study	Mean 15 years	RISP and quetiapine showed similar efficacy in reducing manic symptoms and aggression
Connor 2008, (99)	CD	RCT	12–17 years	No significant differences in Quetiapine's effect on aggression
Yip 2020, (100)	Varied diagnoses	Retrospective chart review	5–17 years	Quetiapine reduced agitation and aggression in the pediatric ED with low rates of EPS
Ziprasidone				
Staller 2004, (101)	Varied diagnoses/ unspecified	Retrospective chart review	8–16 years	IM ziprasidone effective for acutely agitated and aggressive inpatient youth
Khan 2006, (102)	Varied diagnoses	Comparative retrospective chart review	<18 years	IM Ziprasidone and IM Olanzapine similar effectiveness in reducing aggression in youth
Barzman 2007, (103)	Varied diagnoses	Retrospective chart review	5–19 years	IM ziprasidone reduced agitation with concerns for over-sedation
Lurasidone				
Loebel 2016, (104)	ASD	RCT	6–17 years	No statistically significant improvement in irritability

*, for medications with few or no RCTs, we also note open trials or chart reviews. ABC, Aberrant Behavior Checklist; ABC-I, Aberrant Behavior Checklist-Irritability Subscale; ARIP, aripiprazole; ASD, autism spectrum disorder; BD, bipolar disorder; CD, conduct disorder; CGI-S, Clinical Global Improvement-Severity; DBPCT, double-blind placebo controlled trial; IM, intramuscular; MOAS, Modified Overt Aggression Scale; ODD, oppositional defiant disorder; PBO, placebo; PDD, pervasive developmental disorder; RISP, Risperidone; RCT, randomized controlled trial.

behavioral therapy and was more effective than placebo in improving aggression (112). A *post hoc* analysis demonstrated the effectiveness of SPN-810 for impulsive aggression through low remission rates (112).

Monitoring safety of anti-psychotic medications

Educating patients and guardians about potential adverse effects is an important part of prescribing any medication and is especially important with medications used to treat aggression due to the risk of weight gain and metabolic changes. For example, weight gain and metabolic changes are common with atypical antipsychotics and require anticipatory education about healthy lifestyle and careful monitoring of weight, body mass index (BMI), and cholesterol and glucose (113). Risperidone can lead to

elevated serum prolactin levels, thus doctors should monitor for symptoms (114). Close monitoring of white blood cell counts is important for patients taking clozapine (93). Sedation and somnolence were also common side effects for antipsychotic medications (99,112).

Valproic acid (VPA)

Several investigators have examined VPA for treating aggression in children and adolescents with and without developmental disabilities. Donovan and colleagues conducted a small double blinded placebo-controlled trial treating youth ages 10–18 with disruptive behavior disorders, explosive temper and mood lability and showed that VPA improved aggression and irritability (20). Steiner and colleagues (115) conducted a study of adolescent males

with CD who were randomized to receive high or low doses of VPA and demonstrated significant improvements in aggression and that those receiving the higher doses had greater overall and self-reported improvement in impulse control. This study was limited by the absence of a placebo control. Blader and colleagues have examined the use of adjunctive VPA in children with ADHD and residual aggression refractory to stimulants treatment (71,116). In the 2009 study, children were first treated with stimulants and those with residual aggression were randomized to receive adjunctive divalproex treatment or placebo. Those treated with adjunctive VPA were more likely to have their aggression remit. In a later and larger study, they randomized children with stimulant refractory aggression to VPA, risperidone or placebo. Those who received VPA or RISP showed higher aggression remission rates compared to the placebo group.

Two groups examining the use of VPA in the developmental disabilities population found mixed results. Hollander and colleagues (117) examined the treatment of irritability and aggression in children aged 5–17 with ASD and high scores on the Overt Aggression Scale and Aberrant Behavior Checklist (ABC)-Irritability scale and found that VPA in comparison to placebo led to significant improvements in irritability but no statistically significant differences in aggression. Another group investigated the use of VPA in children and adolescents age 6–20 with Pervasive Developmental Disorders (PDD) and significant aggression (118) and found that VPA was not more effective than placebo in treating aggression and irritability.

Taken as a whole, there is some evidence supporting the efficacy of VPA in treating aggression in children with ADHD refractory to stimulant monotherapy, in children with disruptive behavior and in children with developmental disabilities and aggression.

Lithium

Malone and colleagues found that lithium was more effective than placebo in treating acute aggression in children and adolescents with CD (119). Three earlier RCTs also demonstrated that lithium lowered aggressive symptoms such as chronic explosiveness, violent behavior, bullying, fighting, temper outbursts amongst inpatient youth with CD and chronic, severe aggression (109,120,121).

Psychopharmacology conclusion

Prior to considering a pharmacologic treatment for aggression, we recommend a comprehensive assessment, behavioral interventions, and evidence-based psychotherapy and psychopharmacology for the primary disorders. In the event that a child has residual impairing aggression, there are multiple medications with evidence for efficacy, although none with FDA indications at this time. Risperidone and stimulants have the most evidence for efficacy and should be considered first-line, followed by valproate, lithium and alpha agonists. Citalopram also has evidence for efficacy in treating irritability associated with DMDD. Studies demonstrate that aripiprazole is effective in treating irritability, but not aggression specifically. For these medications, one must weigh the risks and benefits, as they may be associated with adverse effects.

Aggression outcomes

Aggression in childhood can have later life correlates. Thus, timely and early management of childhood aggression can play a crucial role in the trajectory of a child's life. Many studies have shown that high levels of physical aggression during the early childhood years can lead to increased violence in later years (5). Children with ODD have a greater risk of developing CD in their teenage years, which puts them at higher risk of developing antisocial personality disorder in adulthood (122,123). Studies that have evaluated the outcomes of juvenile delinquents, such as the Pittsburgh Youth Study, have found that young adults who are involved with criminal offenses continue these behaviors, with increasing frequency, as adults (124). Other studies have shown a correlation with childhood aggression and the development of depression and anxiety disorders as adults (125) demonstrating the connection between aggression with internalizing as well as externalizing disorders. Aggressive behavior during the younger years also increases the risk of developing difficulties with social functioning in adulthood. These individuals tend to have poor outcomes in their relationships with their families, significant others, and peers (125). In addition to the disruption in social functioning, aggression that persists through adolescence into adulthood can negatively impact an individual's physical health. Some criminological theories have elucidated a connection between juvenile delinquency

and poor health in adulthood, including cardiovascular and neurological conditions (126). These long-term effects demonstrate the importance of early detection and intervention in children in order to mitigate poor outcomes in adulthood.

Conclusions

In this selective review, we addressed types and causes of aggression, components of comprehensive assessment and treatment, when managing youth with aggression, and reviewed the most recent evidence-based psychotherapeutic and pharmacological treatments for aggression. Causes of aggression are multifactorial, and thus assessment should be done carefully and take a comprehensive approach. Since aggression is a symptom, and not a diagnosis or underlying cause, a comprehensive assessment taking into account the bio-psycho-social contributors is paramount for identifying the best treatment approach. Treatment involves building a careful alliance with the child and family, treating the primary disorder with evidence-based psychotherapies and medications and using psychotherapeutic and behavioral interventions to target aggression. This approach often leads to decreased aggression. However, if aggression persists, several medications have demonstrated efficacy in treating aggression. These medications may come with adverse effects, thus require careful monitoring, and periodic consideration of discontinuation. With the right knowledge and team, aggression may be managed in a pediatric primary care setting.

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