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Management of Children With Autism Spectrum Disorders

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dence and quality of life, and alleviate family distress. Facilitating development and learning, promoting socialization, reducing maladaptive behaviors, and educating and supporting families can help accomplish these goals. Ideally, interventions should help mitigate the core features of ASDs, which include impairment in social reciprocity, deficits in communication, and restricted, repetitive behavioral repertoire.

Educational interventions, including behavioral strategies and habilitative therapies, are the cornerstones of management of ASDs. These interventions address communication, social skills, daily-living skills, play and leisure skills, academic achievement, and maladaptive behaviors.

Optimization of medical care is also likely to have a positive impact on habilitative progress and quality of life. In addition to routine preventive care and treatment of acute illnesses, management of sleep dysfunction, coexisting challenging behaviors or psychiatric conditions, and associated medical problems, such as seizures, may be particularly important. Medications have not been proven to correct the core deficits of ASDs and are not the primary treatment. However, associated maladaptive behaviors or psychiatric comorbidities may interfere with educational progress, socialization, health or safety, and quality of life. These behaviors may be amenable to psychopharmacologic intervention or, in some cases, treatment of underlying medical conditions that are causing or exacerbating the behaviors. Effective medical management may allow a child with an ASD to benefit more optimally from educational interventions.

EDUCATIONAL INTERVENTIONS

Education has been defined as the fostering of acquisition of skills and knowledge to assist a child to develop independence and personal responsibility; it encompasses not only academic learning but also socialization, adaptive skills, communication, amelioration of interfering behaviors, and generalization of abilities across multiple environments.[9] Physicians and other clinicians are often in a position to guide families to empirically supported practices and help them evaluate the appropriateness of the educational services that are being offered.

Comprehensive Programs for Young Children

In the last 2 decades, research and program development in the area of educational intervention have focused largely on very young children with ASDs because of earlier identification and evidence that early intensive intervention may result in substantially better outcomes.[9,10] Model early childhood educational programs for children with ASDs have been described in thorough reviews.[9,11,12] These model programs are often categorized as behavior analytic, developmental, or structured teaching on the basis of the primary philosophical orientation. Although the approaches have important differences, they also overlap. For example, contemporary comprehensive behavioral curricula borrow from developmental or cognitive approaches (such as addressing joint attention, reciprocal imitation, symbolic play, and theory of mind and using indirect language stimulation and contingent imitation techniques), and some developmental models (eg, the Denver model) and the structured teaching approach of the Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) program use behavioral techniques to fulfill their curriculum goals.[10,13]

Although programs may differ in philosophy and relative emphasis on particular strategies, they share many common goals, and there is a growing consensus that important principles and components of effective early childhood intervention for children with ASDs include the following[9,10,14–16]:

- entry into intervention as soon as an ASD diagnosis is seriously considered rather than deferring until a definitive diagnosis is made;
- provision of intensive intervention, with active engagement of the child at least 25 hours per week, 12 months per year, in systematically planned, developmentally appropriate educational activities designed to address identified objectives;
- low student-to-teacher ratio to allow sufficient amounts of 1-on-1 time and small-group instruction to meet specific individualized goals;
- inclusion of a family component (including parent training as indicated);
- promotion of opportunities for interaction with typically developing peers to the extent that these opportunities are helpful in addressing specified educational goals;
- ongoing measurement and documentation of the individual child's progress toward educational objectives, resulting in adjustments in programming when indicated;
- incorporation of a high degree of structure through elements such as predictable routine, visual activity schedules, and clear physical boundaries to minimize distractions;
- implementation of strategies to apply learned skills to new environments and situations (generalization) and to maintain functional use of these skills; and
- use of assessment-based curricula that address:
  - functional, spontaneous communication;
  - social skills, including joint attention, imitation, reciprocal interaction, initiation, and self-management;

- functional adaptive skills that prepare the child for increased responsibility and independence;
- reduction of disruptive or maladaptive behavior by using empirically supported strategies, including functional assessment;
- cognitive skills, such as symbolic play and perspective taking; and
- traditional readiness skills and academic skills as developmentally indicated.

Specific Strategies

A variety of specific methodologies are used in educational programs for children with ASDs. Detailed reviews of intervention strategies to enhance communication,[9,17–20] teach social skills,[21–24] and reduce interfering maladaptive behaviors[21,25,26] have been published in recent years. Brief descriptions of selected methodologies are provided below.

Applied Behavior Analysis

Applied behavior analysis (ABA) is the process of applying interventions that are based on the principles of learning derived from experimental psychology research to systematically change behavior and to demonstrate that the interventions used are responsible for the observable improvement in behavior. ABA methods are used to increase and maintain desirable adaptive behaviors, reduce interfering maladaptive behaviors or narrow the conditions under which they occur, teach new skills, and generalize behaviors to new environments or situations. ABA focuses on the reliable measurement and objective evaluation of observable behavior within relevant settings including the home, school, and community. The effectiveness of ABA-based intervention in ASDs has been well documented through 5 decades of research by using single-subject methodology[21,25,27,28] and in controlled studies of comprehensive early intensive behavioral intervention programs in university and community settings.[29–40] Children who receive early intensive behavioral treatment have been shown to make substantial, sustained gains in IQ, language, academic performance, and adaptive behavior as well as some measures of social behavior, and their outcomes have been significantly better than those of children in control groups.[31–40]

Highly structured comprehensive early intervention programs for children with ASDs, such as the Young Autism Project developed by Lovaas[35,41] at the University of California Los Angeles, rely heavily on discrete trial training (DTT) methodology, but this is only one of many techniques used within the realm of ABA. DTT methods are useful in establishing learning readiness by teaching foundation skills such as attention, compliance, imitation, and discrimination learning, as well as a variety of other skills. However, DTT has been criticized because of problems with generalization of learned behaviors to spontaneous use in natural environments and because the highly structured teaching environment is not representative of natural adult-child interactions. Traditional ABA techniques have been modified to address these issues. Naturalistic behavioral interventions, such as incidental teaching and natural language paradigm/pivotal response training, may enhance generalization of skills.[13]

Functional behavior analysis, or functional assessment, is an important aspect of behaviorally based treatment of unwanted behaviors. Most problem behaviors serve an adaptive function of some type and are reinforced by their consequences, such as attainment of (1) adult attention, (2) a desired object, activity, or sensation, or (3) escape from an undesired situation or demand. Functional assessment is a rigorous, empirically based method of gathering information that can be used to maximize the effectiveness and efficiency of behavioral support interventions.[42] It includes formulating a clear description of the problem behavior (including frequency and intensity); identifying the antecedents, consequences, and other environmental factors that maintain the behavior; developing hypotheses that specify the motivating function of the behavior; and collecting direct observational data to test the hypothesis. Functional analysis also is useful in identifying antecedents and consequences that are associated with increased frequency of desirable behaviors so that they can be used to evoke new adaptive behaviors.

Structured Teaching

The TEACCH method, developed by Schopler and colleagues,[43] emphasizes structure and has come to be called "structured teaching." Important elements of structured teaching include organization of the physical environment, predictable sequence of activities, visual schedules, routines with flexibility, structured work/activity systems, and visually structured activities.[43] There is an emphasis on both improving skills of individuals with ASDs and modifying the environment to accommodate their deficits. Several reports have documented progress in children who have received TEACCH services as well as parent satisfaction and improvement in parent teaching skills, but these reports were not from controlled studies of treatment outcomes.[44–49] In a controlled trial, Ozonoff and Cathcart[50] found that children treated with a TEACCH-based home program for 4 months in addition to their local day treatment programs improved significantly more than children in the control group who received local day treatment services only.

Developmental Models

Developmental models are based on use of developmental theory to organize hypotheses regarding the fundamental nature of ASDs and design approaches to address

the deficits. The Denver model, for example, is based largely on remediating key deficits in imitation, emotion sharing, theory of mind, and social perception by using play, interpersonal relationships, and activities to foster symbolic thought and teach the power of communication.[12] This program has shifted from a center-based treatment unit to service delivery in homes and inclusive school environments. Several studies have demonstrated improvements in cognitive, motor, play, and social skills beyond what would be expected on the basis of initial developmental rates in children who are treated according to the Denver model, but controlled trials are lacking.[51–54]

Relationship-focused early intervention models include Greenspan and Wieder's developmental, individual-difference, relationship-based (DIR) model,[55] Gutstein and Sheely's relationship-development intervention (RDI),[56] and the responsive-teaching (RT) curriculum developed by Mahoney et al.[57,58] The DIR approach focuses on (1) "floor-time" play sessions and other strategies that are purported to enhance relationships and emotional and social interactions to facilitate emotional and cognitive growth and development and (2) therapies to remediate "biologically based processing capacities," such as auditory processing and language, motor planning and sequencing, sensory modulation, and visual-spatial processing. Published evidence of the efficacy of the DIR model is limited to an unblinded review of case records (with significant methodologic flaws, including inadequate documentation of the intervention, comparison to a suboptimal control group, and lack of documentation of treatment integrity and how outcomes were assessed by informal procedures[55]) and a descriptive follow-up study of a small subset (8%) of the original group of patients.[59] RDI focuses on activities that elicit interactive behaviors with the goal of engaging the child in a social relationship so that he or she discovers the value of positive interpersonal activity and becomes more motivated to learn the skills necessary to sustain these relationships.[56] Some reviewers have praised the face validity of this model, which targets the core impairment in social reciprocity. However, the evidence of efficacy of RDI is anecdotal; published empirical scientific research is lacking at this time. One study reported beneficial effects of RT on young children with ASDs or other developmental disabilities.[58] Parents were taught to use RT strategies to encourage their children to acquire and use pivotal developmental behaviors (attention, persistence, interest, initiation, cooperation, joint attention, and affect). Children in both groups improved significantly on nonstandardized play-based measures of cognition and communication and standardized parent ratings of socioemotional functioning. Although a control group was lacking and the potential role of concurrent educational services was unclear, the improvements were beyond what the authors expected from maturational factors alone.[58]

Speech and Language Therapy

A variety of approaches have been reported to be effective in producing gains in communication skills in children with ASDs.[9,17,20] Didactic and naturalistic behavioral methodologies (eg, DTT, verbal behavior, natural language paradigm, pivotal response training, milieu teaching) have been studied most thoroughly, but there is also some empirical support for developmental-pragmatic approaches (eg, Social Communication Emotional Regulation Transactional Support, Denver model, RDI, Hanen model).

People with ASDs have deficits in social communication, and treatment by a speech-language pathologist usually is appropriate. Most children with ASDs can develop useful speech, and chronologic age, lack of typical prerequisite skills, failure to benefit from previous language intervention, and lack of discrepancy between language and IQ scores should not exclude a child from receiving speech-language services.[60] However, traditional, low-intensity pull-out service delivery models often are ineffective, and speech-language pathologists are likely to be most effective when they train and work in close collaboration with teachers, support personnel, families, and the child's peers to promote functional communication in natural settings throughout the day.[60]

The use of augmentative and alternative communication modalities, including gestures, sign language, and picture communication programs, often is effective in enhancing communication.[17,20,61] The Picture Exchange Communication System (PECS)[62,63] is used widely. The PECS method incorporates ABA and developmental-pragmatic principles, and the child is taught to initiate a picture request and persist with the communication until the partner responds. Some nonverbal people with ASDs may benefit from the use of voice-output communication aids, but published evidence for these aids is scant.[20,64] Introduction of augmentative and alternative communication systems to nonverbal children with ASDs does not keep them from learning to talk, and there is some evidence that they may be more stimulated to learn speech if they already understand something about symbolic communication.[61,62,65]

Social Skills Instruction

There is some objective evidence to support traditional and newer naturalistic behavioral strategies and other approaches to teaching social skills.[22–24,66–68] Joint attention training may be especially beneficial in young, preverbal children with ASDs, because joint attention behaviors precede and predict social language development.[69,70] A recent randomized, controlled trial demonstrated that joint attention and symbolic play skills can be taught and that these skills generalize to different

settings and people.[71] Families can facilitate joint attention and other reciprocal social interaction experiences throughout the day in the child's regular activities. Examples of these techniques are described in the American Academy of Pediatrics parent booklet "*Understanding Autism Spectrum Disorders.*"[72]

A social skills curriculum should target responding to the social overtures of other children and adults, initiating social behavior, minimizing stereotyped perseverative behavior while using a flexible and varied repertoire of responses, and self-managing new and established skills.[10] Social skills groups, social stories, visual cueing, social games, video modeling, scripts, peer-mediated techniques, and play and leisure curricula are supported primarily by descriptive and anecdotal literature, but the quantity and quality of research is increasing.[10,15,73] A number of social skills curricula and guidelines are available for use in school programs and at home.[10,66,74,75]

Occupational Therapy and Sensory Integration Therapy

Traditional occupational therapy often is provided to promote development of self-care skills (eg, dressing, manipulating fasteners, using utensils, personal hygiene) and academic skills (eg, cutting with scissors, writing). Occupational therapists also may assist in promoting development of play skills, modifying classroom materials and routines to improve attention and organization, and providing prevocational training. However, research regarding the efficacy of occupational therapy in ASDs is lacking. Sensory integration (SI) therapy often is used alone or as part of a broader program of occupational therapy for children with ASDs. The goal of SI therapy is not to teach specific skills or behaviors but to remediate deficits in neurologic processing and integration of sensory information to allow the child to interact with the environment in a more adaptive fashion. Unusual sensory responses are common in children with ASDs, but there is not good evidence that these symptoms differentiate ASDs from other developmental disorders, and the efficacy of SI therapy has not been demonstrated objectively.[76–78] Available studies are plagued by methodologic limitations, but proponents of SI note that higher-quality SI research is forthcoming.[79] "Sensory" activities may be helpful as part of an overall program that uses desired sensory experiences to calm the child, reinforce a desired behavior, or help with transitions between activities.

Comparative Efficacy of Educational Interventions for Young Children

All treatments, including educational interventions, should be based on sound theoretical constructs, rigorous methodologies, and empirical studies of efficacy.[15] Proponents of behavior analytic approaches have been the most active in using scientific methods to evaluate their work, and most studies of comprehensive treatment programs that meet minimal scientific standards involve treatment of preschoolers using behavioral approaches.[16,38] However, there is still a need for additional research, including large controlled studies with randomization and assessment of treatment fidelity. Empirical scientific support for developmental models and other interventions is more limited, and well-controlled systematic studies of efficacy are needed.

Most educational programs available to young children with ASDs are based in their communities, and often, an "eclectic" treatment approach is used, which draws on a combination of methods including applied behavior analytic methods such as DTT; structured teaching procedures; speech-language therapy, with or without picture communication or related augmentative or alternative communication strategies; SI therapy; and typical preschool activities. Three studies that compared intensive ABA programs (25–40 hours/week) to equally intensive eclectic approaches have suggested that ABA programs were significantly more effective.[31,32,34] Another study that involved children with ASDs and global developmental delay/mental retardation retrospectively compared a less intensive ABA program (mean: 12 hours) to a comparably intensive eclectic approach and found statistically significant but clinically modest outcomes that favored those in the ABA group.[33] Although the groups of children were similar on key dependent measures before treatment began, these studies were limited because of parent-determined rather than random assignment to treatment group. Additional studies to evaluate and compare educational treatment approaches are warranted.

Programs for Older Children and Adolescents

Some model programs provide programming throughout childhood and into adulthood.[11] More commonly, the focus of specialized programs is on early childhood, and published research evaluating comprehensive educational programs for older children and adolescents with ASDs is lacking. However, there is empirical support for the use of certain educational strategies, particularly those that are based on ABA, across all age groups to increase and maintain desirable adaptive behaviors, reduce interfering maladaptive behaviors or narrow the conditions under which they occur, teach new skills, and generalize behaviors to new environments or situations.[13,21,28]

When children with ASDs move beyond preschool and early elementary programs, educational intervention continues to involve assessment of existing skills, formulation of individualized goals and objectives, selection and implementation of appropriate intervention strategies and supports, assessment of progress, and adaptation of teaching strategies as necessary to enable students to acquire target skills. The focus on achieving social communication competence, emotional and be-

havioral regulation, and functional adaptive skills necessary for independence continues. Educational programs should be individualized to address the specific impairments and needed supports while capitalizing on the child's assets rather than being based on a particular diagnostic label.

Specific goals and objectives and the supports that are required to achieve them are listed in a child's individualized education plan and should be the driving force behind decisions regarding the most appropriate, least restrictive classroom placement. Appropriate settings may range from self-contained special education classrooms to full inclusion in regular classrooms. Often, a mix of specialized and inclusive experience is appropriate. Even highly functioning students with ASDs often require accommodations and other supports such as provision of explicit directions, modification of classroom and homework assignments, organizational supports, access to a computer and word-processing software for writing tasks, and social communication skills training. When a paraprofessional aide is assigned, it is important that there be an infrastructure of expertise and support for the child beyond the immediate presence of the aide.[80] The specific duties of the aide should be outlined, the strategies to be used should be defined, and the aide should receive adequate training.

In adolescence, the term "transition" is used to describe the movement from child-centered activities to adult-oriented activities. The major transitions are from the school environment to the workplace and from home to community living. In schools, transition-planning activities may begin at as early as 14 years of age, and by 16 years of age, the individualized education plan should include an individualized transition plan. The emphasis may shift from academic to vocational services and from remediating deficits to fostering abilities. A vocational assessment is often conducted to evaluate the adolescent's interests and strengths and to determine the services and supports needed to promote independence in the workplace and in the community. Comprehensive transition planning involves the student, parents, teachers, the medical home, and representatives from all concerned community agencies. Depending on the individual's cognitive level, social skills, health condition, work habits, and behavioral challenges, preparation for competitive, supported, or sheltered employment is targeted. Regardless of the type of employment, attention to skill development should never stop. Skills necessary for independent living should be taught to the degree possible given the abilities of the person. Sexuality education instruction should be included, and there is a growing body of literature that has addressed the topic.[81–83]

MEDICAL MANAGEMENT

Children with ASDs have the same basic health care needs as children without disabilities and benefit from the same health-promotion and disease-prevention activities, including immunizations. In addition, they may have unique health care needs that relate to underlying etiologic conditions, such as fragile X syndrome or tuberous sclerosis, or to other conditions, such as epilepsy, that often are associated with ASDs. Those with pica or persistent mouthing of fingers or objects should be monitored for elevated blood lead concentrations, particularly if the history suggests potential for environmental exposure.[84] These health care needs are most appropriately met within the context of a medical home.[85,86]

To deliver appropriate and effective medical care, the history, approach to the patient, physical evaluation, and treatment options must be considered in the context of the patient's ASD.[87,88] Familiarizing the patient with the office setting and staff, allowing ample time while talking before touching the patient, allowing the child to manipulate instruments and materials, keeping instructions simple, using visual cues and supports, slowing down the pace, exaggerating social cues, and having family and/or familiar staff available may be helpful in reducing the obstacles to health care provision presented by patients' difficulties with social interaction, communication, and accepting novelty.[88] Often, more time is required for outpatient appointments. In a nationally representative sample, it was found that children with ASDs spent twice as much time with the physician per outpatient visit compared with children in control groups.[89]

Associated Morbidity and Mortality

Health care utilization and costs are substantially higher for children and adolescents with ASDs compared with children without ASDs,[89–91] and available data suggest that mortality is increased as well (standardized mortality ratio: 2.4–2.6).[92,93] The increased mortality in ASDs is thought to be largely, but not completely, accounted for by the increased mortality associated with mental retardation and epilepsy. Cases of suicide in higher-functioning individuals have been reported.[6]

Seizures

The reported prevalence of epilepsy among people with ASDs ranges from 11% to 39%.[94] Comorbid severe global developmental delay/mental retardation and motor deficits are associated with a high prevalence of seizures (42%),[95] whereas the prevalence of seizures is only 6% to 8% in children with ASDs without severe mental retardation, a motor deficit, an associated etiologic medical disorder, or a positive family history of epilepsy.[95,96] The prevalence of epilepsy also was higher in studies that included adolescents and young adults, because the onset of epilepsy in ASDs has 2 peaks: 1 before 5 years of age and another in adolescence.[97] Anticonvulsant treatment in children with ASDs is based on the same criteria that are used for other children with

epilepsy, including accurate diagnosis of the particular seizure type.[98]

Epileptiform abnormalities on electroencephalography (EEG) are common in children with ASDs, with reported frequencies ranging from 10% to 72%.[99] Some studies have suggested that epileptiform abnormalities on EEG[100] and/or epilepsy[101] are more common in the subgroup of children with ASDs who have a history of regression, whereas other studies have not demonstrated this association.[102,103] Autistic regression with epileptiform abnormalities on EEG has been compared by analogy with Landau-Kleffner syndrome and electrical status epilepticus in sleep, but there are important differences between these conditions, and the treatment implications are unclear.[94,104] Whether subclinical seizures have adverse effects on language, cognition, and behavior is debated, and there is no evidence-based recommendation for the treatment of children with ASDs and epileptiform abnormalities on EEG, with or without regression.[104] Universal screening of patients with ASDs by EEG in the absence of a clinical indication is not currently supported.[2,99] However, because of the increased prevalence of seizures in this population, a high index of clinical suspicion should be maintained, and EEG should be considered when there are clinical spells that might represent seizures.

Gastrointestinal Problems

The relationship between gastrointestinal problems and ASDs is unclear, because most studies have not examined representative groups of children with ASDs compared with appropriate controls.[105,106] Surveys published in the gastroenterology literature have stated that gastrointestinal problems, such as chronic constipation or diarrhea, occur in 46% to 85% of children with ASDs.[107–109] Lower rates in the range of 17% to 24% have been reported in other population-based studies,[110–112] and a nested case-control study in the United Kingdom found that only 9% of children with ASDs and the same percentage of controls had a history of gastrointestinal complaints.[113] However, in a recent cross-sectional study that used structured interviews and matched control groups, a lifetime history of gastrointestinal symptoms (including abnormal stool pattern, frequent constipation, frequent vomiting, and frequent abdominal pain) was elicited in 70% of the children with ASDs, compared with 42% of the children with other developmental disabilities ($P = .03$) and 28% of the children without developmental disabilities ($P < .001$).[114]

In children with ASDs undergoing endoscopy, who may or may not be representative of the general population of children with ASDs, high rates of lymphoid nodular hyperplasia and, often, histologically subtle esophagitis, gastritis, duodenitis, and colitis have been described, and preliminary evidence suggests that some immunohistochemical features may be unique to inflammation associated with ASDs.[105,115,116] The existing literature does not support routine specialized gastroenterological testing for asymptomatic children with ASDs.[105] However, if a child with an ASD presents with symptoms such as chronic or recurrent abdominal pain, vomiting, diarrhea, or constipation, it is reasonable to evaluate the gastrointestinal tract. Occult gastrointestinal discomfort also should be considered in a child who presents with a change in behavior, such as outbursts of aggression or self-injury. Radiographic evidence of constipation has been found to be more common in children with ASDs than in controls with abdominal pain (36% vs 10%),[117] and effective management may provide global benefit.

Sleep Disturbance

Sleep problems are common in children and adolescents with ASDs at all levels of cognitive functioning.[118–122] Sleep problems correlate with family distress and may have significant effects on daytime functioning and quality of life of children with ASDs.[123–125] In some cases, there may be an identifiable etiology such as obstructive sleep apnea or gastroesophageal reflux; assessment and treatment are guided by history and physical examination. When there is not an identifiable medical cause, behavioral interventions including sleep-hygiene measures, restriction of daytime sleep, positive bedtime routines, and extinction procedures often are effective.[118,126–129]

Relatively little empirical information is available regarding pharmacologic management of sleep problems in children with ASDs or other developmental disabilities. Recommendations typically are based on case reports and open-label trials, extrapolation from the adult literature, and expert consensus (Table 1).[128] There is some evidence of abnormality of melatonin regulation in children with ASDs,[125,130] and melatonin may be effective for improving sleep onset in children with ASDs as well as children with other developmental disabilities[131–134] and otherwise healthy children with sleep/wake disorders.[135] A recent open-label study suggested that controlled-release melatonin improved sleep in a group of 25 children with ASDs and that treatment gains were maintained at 1- and 2-year follow-up,[136] but randomized, double-blind, placebo-controlled studies are needed. Recently, a child and a young adult with ASDs with significant insomnia were reported to have responded well, with no apparent adverse effects, to open-label treatment with the high-affinity melatonin receptor agonist ramelteon.[137] Antihistamines, α_2-agonists, benzodiazepines, chloral hydrate, trazodone, and newer nonbenzodiazepine hypnotic agents, such as zolpidem and zaleplon, sometimes are used to treat pediatric insomnia.[128] In some cases, other conditions or symptoms, such as epilepsy, depression, anxiety, or aggressive outbursts, warrant pharmacologic treatment, and an agent that also may assist with sleep can be chosen.[118]

TABLE 1 Selected Potential Medication Options for Common Target Symptoms or Coexisting Diagnoses in Children With ASDs

Target Symptom Cluster	Potential Coexisting Diagnoses	Selected Medication Considerations	Selected References
Repetitive behavior, behavioral rigidity, obsessive-compulsive symptoms	Obsessive-compulsive disorder, stereotypic movement disorder	SSRIs (fluoxetine,[a] fluvoxamine,[a] citalopram, escitalopram, paroxetine, sertraline)	McDougle et al,[158,b] Buchsbaum et al,[180,b] Sugie et al,[159,b] Hollander et al,[157,b] Moore et al,[160,c] Namerow et al,[181,d] Owley et al[182,d]
		Atypical antipsychotic agents (risperidone,[a] aripiprazole, olanzapine, quetiapine, ziprasidone)	McDougle et al[164,b]
		Valproic acid[a]	Hollander et al[183,b]
Hyperactivity, impulsivity, inattention	Attention-deficit/hyperactivity disorder	Stimulants (methylphenidate,[a] dextroamphetamine, mixed amphetamine salts)	Quintana et al,[168,b] Handen et al,[169,b] RUPP Autism Network[170,b]
		α_2-agonists (clonidine,[a] guanfacine)	Fankhauser et al,[172,b] Jaselskis et al,[173,b] Posey et al,[175,d] Scahill et al (RUPP Autism Network)[174,d]
		Atomoxetine[a]	Arnold et al,[178,b] Jou et al,[176,d] Posey et al[177,d]
		Atypical antipsychotic agents (risperidone,[a] aripiprazole, olanzapine,[a] quetiapine, ziprasidone)	McCracken et al,[162,b] Arnold et al,[163,b] Shea et al,[165,b] RUPP Autism Network,[166,b] Troost et al[167,d]
Aggression, explosive outbursts, self-injury	Intermittent explosive disorder	Atypical antipsychotic agents (risperidone,[a] aripiprazole, olanzapine, quetiapine, ziprasidone)	McCracken et al,[162,b] Arnold et al,[163,b] Shea et al,[165,b] RUPP Autism Network,[166,b] Troost et al[167,d]
		α_2-agonists (clonidine,[a] guanfacine)	Fankhauser et al,[172,b] Jaselskis et al,[173,b] Posey et al[175,d]
		Anticonvulsant mood stabilizers (levetiracetam, topiramate, valproic acid)	Hollander et al[184,d], Rugino and Samsock[185,d], Hardan et al[186,d], Myers[149,c], Myers and Challman[149,c]
		SSRIs (fluoxetine,[a] fluvoxamine,[a] citalopram, escitalopram, paroxetine, sertraline)	McDougle et al,[158,b] Moore et al,[160,c] Namerow et al,[181,d] Owley et al[182,d]
		β-blockers (propranolol, nadolol, metoprolol, pindolol)	Connor et al,[187,d] Ratey et al,[188,d] Myers and Challman[149,c]
Sleep dysfunction	Circadian rhythm sleep disorder, dyssomnia–not otherwise specified	Melatonin	Giannotti et al,[136,d] Ian and Freeman,[131,c] Phillips and Appleton,[133,c] Turk,[134,c] Owens et al[128,c]
		Ramelteon	Stigler et al[137,e]
		Antihistamines (diphenhydramine, hydroxyzine)	Reed and Findling,[189,c] Owens et al[128,c]
		α_2-agonists (clonidine, guanfacine)	Mehta et al,[190,d] Ingrassia and Turk,[191,d] Posey et al,[175,d] Owens et al[128,c]
		Mirtazapine	Posey et al[192,d]
Anxiety	Generalized anxiety disorder, anxiety disorder–not otherwise specified	SSRIs (fluoxetine,[a] fluvoxamine,[a] citalopram, escitalopram, paroxetine, sertraline)	McDougle et al,[158,b] Buchsbaum et al,[180,b] Sugie et al,[159,b] Hollander et al,[157,b] Moore et al,[160,c] Namerow et al,[181,d] Owley et al[182,d]
		Buspirone	Buitelaar et al[193,d]
		Mirtazapine	Posey et al[192,d]
Depressive phenotype (marked change from baseline including symptoms such as social withdrawal, irritability, sadness or crying spells, decreased energy, anorexia, weight loss, sleep dysfunction)	Major depressive disorder, depressive disorder–not otherwise specified	SSRIs (fluoxetine,[a] fluvoxamine,[a] citalopram, escitalopram, paroxetine, sertraline)	McDougle et al,[158,b] Moore et al,[160,c] Namerow et al,[181,d] Owley et al[182,d]
		Mirtazapine	Posey et al[192,d]

Evaluation of Challenging Behaviors

Problematic emotional reactions and behaviors such as aggression and self-injury are common in children and adolescents with ASDs. In some cases, medical factors may cause or exacerbate maladaptive behaviors, and recognition and treatment of medical conditions may eliminate the need for psychopharmacologic agents. For example, in the case of an acute onset or exacerbation of aggressive or self-injurious behavior, a source of pain or discomfort may be identified and treated.[138] Sources of discomfort may include otitis media, otitis externa, pharyngitis, sinusitis, dental abscess, constipation, urinary