Autism Spectrum Disorders: Early Detection, Intervention, Education, and Psychopharmacological Management

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Our understanding and treatment of children with autism have changed dramatically since Leo Kanner first formally documented the disorder in 1943.

With reference to the historical context, this paper reviews recent research addressing 4 major issues: early detection, intervention, education, and psychopharmacological management of children with autism and related (autistic) spectrum disorders (hereafter, "autism").

We conclude from our review of the evidence that, in the absence of additional, more compelling data, the clinical usefulness of existing screening instruments remains questionable. However, the potential importance of such research is underscored by the clear benefits of early behavioural intervention: despite differences in orientation, outcomes for children with autism can be significantly enhanced with early intensive intervention. Although many questions remain (notably, What are the critical therapeutic components? For whom? For what domains of development? For what level of intensity and duration?), interventions shown to be effective are all carefully planned, engineered, monitored, and designed to target specific skill domains. Including children with autism in regular classes within the public school system poses several challenges, the most pressing of which is the large number of school personnel who need to be trained in evidence-based teaching and behavioural management practices. Finally, psychotropic drugs may help to reduce some symptoms, but they are neither curative nor a substitute for other forms of support and intervention.

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Clinical Implications

- Currently, the early detection of autism is limited by the lack of early-screening instruments that are sensitive as well as specific to autism.
- The demonstrated effectiveness of early intensive intervention for children with autism warrants its widespread practice.
- Psychotropic drugs should be used judiciously in the treatment of children with autism.

Limitations

- Space limitations precluded a detailed review of some issues; however, we provide relevant references.
- Our review is also limited by the lack of data on some issues.

Key Words: *autism, autistic spectrum disorders, early detection, early screening, early intervention, intensive behavioural intervention, education, psychopharmacological management*

Autism has traditionally been viewed as a severe but rare disorder for which little can be done. Following Kanner's initial description (1) and well into the 1970s, the dominant view was that autism's causes were psychological and that treatment should necessarily focus on the psychopathological consequences of faulty parenting (2). This conceptualization of autism was counter-therapeutic and also failed to promote a scientific approach to understanding and treating the condition. The tide began to change in the 1960s, when a handful of innovative thinkers challenged prevailing dogma. In their view, corroborated by a link with epilepsy (3,4), autism was a neurological disorder affecting development of the brain and its associated functions and warranting careful scientific study (5–8).

With this change in orientation, research efforts began to focus on understanding autism's nature and origins and on identifying effective treatment methods. Among the most significant of the early contributions were the elegant and insightful experiments conducted by Beate Hermelin and Neil O'Connor (9); these studies provided clear evidence for information processing deficits in autism. These deficits included lower-level sensory and perceptual impairments and difficulties in deriving meaning from language. At the same time, Eric Schopler revolutionized our approach to the treatment of children with autism (10,11). Consistent with evidence of information-processing deficits, his groundbreaking work showed that therapeutic gains were achieved by adopting a pedagogical approach: children with autism learn and develop through structured teaching and the use of positive behavioural principles.

The 1980s were marked by an additional discovery that has transformed the field. Since Kanner's original description (1), our conceptualization of autism has been based largely on its prototype (also known as classic autism); that is, the relatively small proportion of children who are distinguished by social aloofness, complex rituals, and insistence on sameness. Thanks, however, to the thoughtful and innovative work of Lorna Wing and her colleagues (12,13), we now recognize that autism is the most extreme form of a spectrum of related disorders (including Asperger syndrome and other less severe autistic variants). As our conceptualization and, hence, definition of autism has broadened, so too have our prevalence estimates (14–17). Recent evidence that autistic spectrum disorders are among the most common of the severe disorders of development (with a prevalence of at least 6 or 7 per 1000; see 18) challenges the most fundamental of our traditional views, as do findings that outcomes can be substantially improved with early, syndrome-specific (that is, behavioural) intervention. On the one hand, the putative benefits of early intervention have underscored that early detection of autism is important. On the other hand, they have generated concern about how best to maintain therapeutic gains and support further development in later childhood and adolescence.

This paper provides an overview of recent evidence on early detection and intervention and on the education and psychopharmacological management of children with autistic spectrum disorders (hereafter, autism). We first discuss the rationale for early detection, describe existing methods, and outline their limitations at present. We then offer an historical overview of early-intervention programs and a critical evaluation of the evidence for treatment effectiveness. Next, we discuss best practices in the education of children with autism and in the pharmacologic treatment of behaviours associated with autism. Throughout, we identify outstanding research questions and take care to outline the clinical or applied implications of recent advances in the field.

Early Detection of Autism

With the advent of standardized diagnostic tools, notably the Autism Diagnostic Interview-Revised (ADI-R) (19,20) and the Autism Diagnostic Observation Schedule-Generic (ADOS-G) (21), expert clinicians are now able to diagnose autism reliably by age 3, and even age 2, years (22). However, evidence indicates that most children are not diagnosed prior to age 4 years, typically at least 2 years after parents first seek professional advice because they are concerned about their child's development (23,24). In the interim before they receive the diagnosis, most children are seen by at least 3 professionals, and parents experience significant distress and frustration. The long delay between parents' initial concerns and eventual diagnosis also postpones appropriate intervention, which, coupled with evidence of its effectiveness (25,26), leaves parents with the sense that precious time has been lost.

Evidence that signs of autism are apparent within the first 2 years of life comes from several sources: parents' retrospective reports (27,28), home videos (29,30), and case studies of children later diagnosed with autism (31). Evidence also comes from a systematic study of 41 high-risk infants (all with a sibling suffering from autism) in which 4 children exhibited distinct autistic signs at age 18 months (32). Such findings, together with autism's severity, its staggering prevalence, and the relative merits of early intervention, all argue for the importance of early detection. Indeed, there is wide agreement that the early detection and treatment of autism is a health care priority (for example, 33). Recent practice parameters issued by the American Academies of Neurology, Pediatrics, and Child and Adolescent Psychiatry represent the work of a multidisciplinary Consensus Panel comprising health care professionals, clinical researchers, and parent organizations.

As outlined by Filipek and others (34), recommendations from the Consensus Panel focus on the importance of 3 levels

of clinical evaluation: assessing the child's risk for autism; confirming the diagnosis; and specifying the intervention warranted, based on the child's unique profile of functional needs. The Consensus Panel also recommend that population-based screening for autism be conducted in 2 stages. The first stage should focus on routine developmental surveillance, including measures designed to detect general developmental delays. The second stage should be designed specifically to detect delayed speech development and other warning signs of autism. The problem, as recognized by Filipek and others and detailed by Zwaigenbaum (35,36), is that early detection of autism is restricted by the limitations of existing screens and, more generally, by our lack of knowledge about the early developmental trajectories symptomatic of autism.

Existing screens for the early detection of autism include the Checklist for Autism in Toddlers (CHAT) (32, see also 37 for a recent modification, the Quantitative CHAT), the Modified-CHAT (M-CHAT) (38), the Screening Test for Autism in Toddlers (STAT) (39), the Pervasive Developmental Disorders Screening Test-II (PDDST-II) (40), and the Early Screening for Autism questionnaire (ESA) (41). While considerable overlap exists in the constructs assessed, these instruments vary in terms of whether they were designed as first- or second-level screens (that is, population-based screening or screening of children referred for developmental concerns, respectively), whether they take the form of a parent questionnaire and (or) direct observation by a general practitioner, and the age at which they are to be administered. We emphasize that existing screens are in the early stages of development; as indicated below, available data (or the lack thereof) underscore both the many outstanding research questions and that caution is warranted in using them clinically.

Of those designed as first-level screens (the CHAT, M-CHAT, PDDST-II, and ESA), the CHAT is the only instrument that has been evaluated in a general population (n = 16 235) and for which prospective follow-up data on misclassification errors allow adequate assessment of predictive value. The CHAT was designed for use with toddlers aged 18 months; it includes both direct observation and parent questionnaire components. Based on preliminary work, it focuses on 3 key items predictive of autism at age 18 months: gaze monitoring, protodeclarative pointing (that is, pointing to show), and pretend play (32). Despite its initial promise and excellent specificity (99.9%), systematic follow-up has indicated that over 80% of children diagnosed by age 7 years are missed by the CHAT at initial age 18 months screening (42–44). Moreover, attempts to modify the cut-off criteria to increase sensitivity (from 18% to 38%) resulted in an unacceptable decrease in positive predictive value (from 75% to 5%).

To improve on the prediction of the CHAT, the M-CHAT (37) includes several additional items that encompass a broader range of developmental domains (notably, sensory and motor abnormalities, social referencing, imitation, and orientation to name called, for a total of 22 items). It also differs from the CHAT in its parent-questionnaire format; in its lack of an observation component; and in its administration at age 24 months, rather than at age 18 months, to capture the subgroup of children who regress between the ages of 18 and 24 months. The M-CHAT has been initially evaluated in a mixed group of toddlers seen for routine checkups by pediatricians or family physicians (n = 1122) or referred for early intervention for language delays or other developmental concerns (n = 171). Estimates of specificity and sensitivity should be treated as preliminary and are likely inflated by the high proportion of cases (36/171 or 21%) in the intervention group and by the lack of follow-up of screen-negative cases (36). Research on the CHAT serves to underscore that many children who develop autism may be missed at the time of the original screen. It also remains to be determined whether administration of the M-CHAT at age 24 months predicts autism in a large general population.

The STAT (39) is a second-level screen designed for children aged 2 to 3 years, who are observed in semistructured playful interactions in an attempt to distinguish those with autism from those with other developmental disorders or concerns. Preliminary data are encouraging (39), but estimates of sensitivity (83%) and specificity (86%) are based on small numbers (specifically, 12 children with autism and 21 with other developmental disorders) and may well be inflated by the methodological limitations outlined above (that is, overrepresentation of autism in the test sample and failure to follow up for misclassification errors; see 36). The PDDST-II (40) includes both a first-level (Stage 1) and second-level (Stage 2) screen, each of which takes the form of a parent questionnaire. The ESA, a first-level screen designed for toddlers aged 14 months, includes parent questions that, when warranted, are followed by direct observation (41). As yet, there are no published data on these latter 2 instruments.

What conclusions can we draw from the evidence to date? Clearly, remarkable progress has been made on the complex but important problem of detecting autism earlier in life. Overall, data on existing measures, particularly the CHAT, suggest that sensitivity may be more of a problem than specificity. In other words, high rates of false negatives (vs false positives) may be a particular challenge. An outstanding question is whether there is real variability in the nature and timing of early signs of autism or whether existing instruments are simply constrained by our lack of knowledge of the diversity in signs evident by a particular age. In either case, we need to identify the critical age(s) at which detection is optimal. The

task is complicated by the need for instruments that, on the one hand, are developmentally appropriate but, conversely, can be used for young children whose developmental levels vary widely (that is, who have varying levels of cognitive, emotional, or motivational impairment). We also need to better understand the potential diversity in early trajectories predictive of autism. To this end, we are conducting a large prospective study of high-risk infants with a sibling suffering from autism, in which several screens are being evaluated (35,36), including our newly developed measure (45) designed to monitor the emergence of autism in even younger and developmentally less advanced infants.

Finally, a major goal of second-level screens is to provide information relevant to triaging children to the most appropriate diagnostic and treatment services as efficiently as possible. It remains to be determined whether the predictive power of existing autism screens will be adequate for this purpose, and in the event that any are, whether or under what particular circumstances this is a cost-effective way to proceed. In the meantime, although we are clearly able to detect cases earlier than was previously possible, these instruments should be used with caution in clinical settings. Indeed, to evaluate their utility, they should ideally be used within a research context. Evidence to date suggests that potentially high miss rates dictate careful monitoring of screen-negative cases to ensure that such children are not misclassified and excluded from services that might optimize their outcomes.

Early Intervention in Autism

Many views of autism have been radically revised by research published over the past 20 years, and one of the most compelling is that psychosocial interventions can change the disorder's course. Until the late 1980s, our understanding of treatment efficacy was limited to short-term interventions focused on manipulating particular behaviours. These early papers documented the efficacy of targeted behavioural interventions for children with autism, both for increasing skill development in a wide range of areas and for decreasing rates and severity of unwanted behaviours (for reviews, see 46,47).

In the late 1980s, however, a new approach to treatment began to be reported: comprehensive early-intervention programs, similar in concept to the early-intervention work developed in the 1970s and 1980s in the US for children from very high-risk backgrounds and for those with mental retardation and other disabilities (for a comprehensive review of relevant research, see 48). Such approaches involved highly focused and individualized teaching activities that targeted all areas of development and were delivered for many hours each week. Several groups with differing approaches reported positive effects from comprehensive early intervention (49–53; for reviews of this work, see 25,26,54).

Several different programs with a developmental orientation have published outcome papers. The Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH) program, classified as a developmental model by its originators, emphasizes instruction that teaches to the strengths that children with autism have in visual-spatial understanding, object manipulation, and enjoyment of highly structured, independent, and routine activities (Web site: http://www.teacch.com). Ozonoff and Cathcart examined the efficacy of a 1-to-1, parent-delivered TEACCH intervention given daily for 1 hour to a group of 11 preschoolers with autism who were already receiving full-day, school-based, behavioural education (55). After approximately 16 weeks of treatment, the children who received the TEAACH intervention had made significant gains in several developmental areas, compared with 11 well-matched, waiting-list control subjects. In addition to significantly improved overall scores on the Psychoeducational Profile-Revised (PEP-R) (56), the TEACCH group had significantly improved imitation, nonverbal perception, cognition, and fine and gross motor skills. This group made 3 to 4 times more progress in months of gain than the comparison subjects, who were getting full-day, intensive behavioural education.

The Denver Model, a second developmental model with published outcome data, emphasizes development of play skills, positive affect, interpersonal relationships, and language development (57). Rogers and colleagues (49,58,59) reported outcomes for a large group of children attending a 5-hour daily specialized group class with 6 children and 3 teaching staff per classroom; also offered were additional speech and language therapy, occupational therapy, and clinical psychology therapy services. Over an intervention period of 6 to 12 months, the group demonstrated statistically significant changes above and beyond the gains expected, based on their initial developmental rates in most areas of development. These included gains in receptive and expressive language, in symbolic play, and in responsivity and positive affect in dyadic interactions with their parents. Their developmental rates doubled during the treatment period and attained the normal rate of 1 month of growth per month of treatment—a rate sustained for as long as they were enrolled in the program. Rogers and DiLalla demonstrated that, during intervention, children with more severe delays achieved the same normal developmental rate as the children with less severe delays and that children with autism progressed at a rate similar to that of a group with developmental delays but without autism also enrolled in the treatment program (51). Finally, Rogers, Lewis, and Reis (60) published a replication study demonstrating that staff of ongoing public intervention classrooms could learn the Denver Model, could deliver it at appropriate levels of model fidelity, and could achieve the same increases

in developmental skills and rates as had the children in the original model program.

The peer-mediated learning of Strain, Odom, and colleagues is another early-treatment approach in autism that demonstrates a convergence of developmental and behavioural foundations. This group has published many single-subject design papers; however, the approach has been developed into a more long-term, integrated classroom design known as the Learning Experiences: an Alternative Program for Preschoolers and Parents (LEAP) preschool model (50). Using a design similar to that of the Denver Model studies, these authors have demonstrated that developmental rates of treated children accelerated to normal levels, with significant gains in virtually all areas of development. Further, long-term follow-up results were positive, with almost 50% of children attending regular school classes (61).

The final developmentally based program to be considered is Greenspan and Wieder's model (62), which has a foundational type of social communication intervention, termed "Floortime," and additional professional services. A review of case files demonstrated positive social and developmental gains, although this study did not include a standard assessment battery. Published reports from various behaviourally based group programs have also documented positive treatment effects, with strong gains in all aspects of learning, particularly in language development. The Walden program at Emory University (63), the work at Rutgers University under the influence of Sandra Harris and colleagues (51), and the work at Princeton, under the current direction of Krantz and McClannahan (52), have been particularly important influences.

The most influential and provocative paper in the literature on early intervention in autism was published by Lovaas and colleagues (64). It described a controlled study of an intensive and comprehensive behavioural approach that delivered 40 hours weekly for 2 or more years during the early preschool period. The approach resulted in remarkable gains in language and IQ, compared with the control group; approximately one-half of the treated children were no longer symptomatic ("recovered"). The empirical design of this study was not flawless, however. While it did include control groups, there were many methodological problems: subjects were not randomly assigned to groups, there was no alternative treatment of comparable intensity, and the measurement of outcomes was limited. Nevertheless, the design was considerably stronger than that of any other study published from this period, and the better outcomes than previously reported may well have reflected the more intensive and longer-term treatment that these children received, compared with other treatment approaches. A follow-up paper by the same group documented these improved outcomes into adolescence (65).

The improved, controlled design of this study; the rather straightforward and easily replicable method for delivering the intervention, described in a published and readily available treatment manual (66); and the much improved status of the treated children profoundly altered views, practices, and standards in the US regarding early intervention for children with autism. This study also raised the bar on methodology, with the result that current outcome studies require the use of a comparison group.

It was necessary to replicate the early-intervention findings to answer the following 2 main questions from the first set of papers: When tighter experimental methods are applied, is the early-intervention effect still evident? Does Lovaas's approach drastically improve outcomes in the treatment group and lead to recovery for a significant subgroup of treated children? Regarding the first question, 2 papers using random assignment and careful designs and an additional paper using wait-list control subjects confirmed that various treatments have both short-term and longer-term positive effects, especially on language and intellectual function. Treatments included a short-term, centre-based, full-day intervention; a 1-to-1, home-based, behavioural intervention that replicated Lovaas's method; and a low-intensity, home-based, parent-delivered intervention (67–69).

To summarize, the literature thus supports the following conclusion: delivering interventions for more than 20 hours weekly that are individualized, well planned, and target language development and other areas of skill development significantly increases children's developmental rates—especially in language—compared with no or minimal treatment. While some of the gain in developmental rates is probably due to children's greater understanding of the testing situation and greater responsiveness to adult instructions, there is clear gain in language, which is the single best predictor of adult outcomes. Further, improved cooperation with adults is probably in itself a crucial outcome variable, given that it is a fundamental mechanism for learning and thus an important effect of early intervention.

Regarding the second question, 2 recent studies with improved designs partly replicated Lovaas's original findings and demonstrated complementary findings. Smith and others used true random assignment of 28 young children to treatment and parent-training comparison groups (69). The groups were well matched at intake and were followed up after 2 years, at which point the treated group outperformed the parent-training group on measures of intelligence, visual-spatial skills, language, and academics, although not on measures of adaptive functioning or behaviour problems. However, there was no recovery associated with the treated group, and the children diagnosed with pervasive developmental disorder not otherwise specified (PDD-NOS) made far

more progress in far more areas than did those diagnosed with autistic disorder, who continued to demonstrate significant impairments in all areas. Eikeseth and others compared the effects of 1 year of Lovaas's treatment to the same amount of eclectic treatment, delivered over the same number of hours and with same staff ratio (70). Both treatments were delivered in a school setting to children with autism, aged 4 to 7 years. The children were not randomly assigned but were carefully matched on all variables. Assignment was based on availability of personnel to supervise treatment and was not influenced by child characteristics or family preference. Group data from the behavioural-treatment group demonstrated significantly larger gains on standardized tests than did data from the eclectic treatment group. This paper demonstrates important effects on older children from treatment delivered in a school setting. Most important, it demonstrates that the intervention effect is not simply attributable to treatment intensity in terms of hours and ratios. Again, however, there is no report of recovery in the treated group. The alternative treatment was an eclectic assortment of interventions delivered at the discretion of the teaching staff, rather than an alternative, systematic, and well-defined treatment. A specific intervention model may for many reasons (for example, it use of a treatment manual, decision tree, or set curriculum) be a more powerful change agent than is an eclectic assortment of teaching techniques.

To summarize, these comparative studies replicated the original findings that groups of children receiving Lovaas's intensive behavioural treatment showed greater group gains in IQ and language than did children in comparison groups, but the studies did not replicate recovery as an outcome of the experimental treatment. Until some study replicates the recovery outcome, it needs to be laid aside in discussions about the effectiveness of early interventions in autism.

The outcome papers as a whole provide a powerful message: the development of young children with autism can be significantly enhanced by the delivery of carefully planned and carefully delivered instruction that targets the specific learning areas of communication, social skills, play, cognition, and independence. The convergence of findings from these theoretically varied approaches has fundamentally changed our view of the nature of developmental impairments in autism by implying more plasticity in course (and, perhaps, a stronger experiential influence on the phenotype) than had been imagined earlier. Several international scientific review groups have separately reviewed this literature, with similar conclusions: outcomes for children with autism can be significantly enhanced by offering many hours weekly of targeted and individualized teaching that is carefully planned, delivered, and monitored (54,71). It seems clear that we must leave behind several truisms about autism, including the assumptions that 50% of affected children will not speak, and 75% will have mental retardation. These older findings need to be considered as reflecting untreated children with autism, rather than as the expected course and outcome for children with autism today. Early intervention in autism needs to be seen as similar to teaching language to deaf children or to teaching mobility and Braille to blind children—a necessary, publicly funded, rehabilitative service, without which outcomes cannot be meaningfully discussed.

New questions now beg to be addressed. How many hours are needed to get optimum effects, and how should those decisions be made? Is one methodology or teaching approach significantly better than another, when all other variables are controlled? At what is it better? If recovery is not an expected outcome, then what are the most important outcomes—social skills, language, tested IQ scores, decreases in autism symptoms, or low levels of maladaptive behaviour? To what extent are these independent outcome variables? Adaptive behaviour, rather than language and IQ, may be the best indicator of outcome in adulthood; however, follow-up to adulthood takes an entire generation of science. Nevertheless, determining the crucial outcome variables is critical, because it is quite conceivable that different intervention approaches will result in different skill profiles in children with autism. It is equally conceivable that the same intervention approaches will result in different profiles of abilities among children with more severe impairments, compared with children having milder impairments. We need to know what kinds of profiles are created by the different main treatments, so that we can begin to make informed decisions.

The next generation of studies needs to compare the effects of different treatments, to isolate the variables accounting for change, and to move beyond group analyses to examine individual response variability within and across treatments. Such studies will require large groups across collaborating sites, which is no easy task. They will also require that those carrying out the studies have expertise in different treatments, that straightforward treatment manuals and fidelity measurement systems for other main treatments be developed, and that key variables differentiating treatments be elucidated. With such studies, we can begin to understand which intervention variables are actually responsible for increasing developmental rates, and in which children. The field needs this level of information to select or construct the most effective potential treatment approach for each young child with autism.

Education of Children With Autism

In Canada, the public education of children with autism has changed dramatically over the past 20 years. Traditionally, such children were placed in segregated classes of relatively small and typically mixed groups of children with mental

handicap, often in schools outside their communities. Beginning in the 1980s, the policy changed largely, if not exclusively, to one of inclusion; most children with autism are now integrated either full- or part-time into regular classes in schools within their communities. Several factors contributed to this change in policy, including strong advocacy on the part of parents whose children suffered from autism. The change reflects the broader social movement toward deinstitutionalization of children and adults with developmental disorders, protection of their rights, and normalization of their lives (72,73). The challenge is how the public education system can ensure that children with autism, like others, have adequate opportunities to socialize, to learn, and to become independent, responsible, and valued members of society.

The public school system is of particular interest, because it is the context in which children and adolescents with autism are generally educated and spend a great deal of their time. Our discussion focuses on current public educational practices and highlights existing challenges and issues of concern, as well as directions for future research efforts. For these purposes, we draw on the 2001 report of the US Committee on Educational Interventions for Children with Autism (54). We refer interested readers to this document for an excellent overview of educational goals, evidence-based interventions, and policy, legal, and research issues in the education of children with autism.

The practice of including children with autism in regular classes brings with it a unique set of challenges, not the least of which is that many educators need to acquire the knowledge and skill base required for developing effective programs. School policy dictates that Individual Education Plans (IEPs) be designed and regularly reviewed by school personnel in consultation with parents, that curricula be modified according to the individual learning needs and styles of each child, and that teacher aides (when available) assist with implementing programs and managing behavioural issues. An issue of central importance here is the question of how programming will proceed; that is, by which precise methods will the identified IEP goals and modified program be realized for each child?

While it is widely recognized that no single program fits all, efforts are increasingly aimed at representing best practices in the socialization and education of children with autism, as derived from the large body of existing research. Evidence-based interventions differ in philosophies, and the methodologies employed are not flawless. Some interventions address broad issues, such as communication training (74), structured teaching (11,75), and behavioural programming (47,76); others are designed for more specific issues, such as social skill development (77,78), academic instruction (79), and the development of life skills (80,81). What they share, however, is that all have been shown to yield substantial benefits not otherwise seen when compared with regular, less structured, and less systematic approaches to teaching children with autism. In the public school system, more widespread use of evidence-based interventions for children with autism would do much to ensure that the developmental gains made in early intervention programs are maintained and that the children will continue to develop new skills during the school years.

Among the challenges identified in the existing literature, 3 bear emphasizing. First, autism is a complex disorder, requiring the input of cross-disciplinary teams of educators and health care professionals, and also of parents. Better coordination of our efforts is needed to ensure more effective and ongoing information sharing and planning, particularly during periods of transition (that is, from preschool programs into schools, from one class and teacher to another, and from high school to beyond). Second, there is a pressing need to train teachers and teacher aides about autism and about using evidence-based methods for teaching and managing behavioural issues. While exposure to relevant readings and conferences may help, these are no substitute for ongoing support from, and problem solving with, others who have the necessary expertise and experience. Finally, there is wide agreement that the social and emotional well being of children with autism needs to receive more attention within the school system. That is, while academic learning is important, this goal should not supersede the children's need for social contact with others, for participation in recreational and other school-based activities, and for a sense of belonging and of being recognized and valued. It is to be hoped that future research efforts will aim to address these important educational issues issues affecting the very large numbers of children with autism served by the public school system.

Psychopharmacological Management

There is no curative treatment for autism, and psychotropic drugs have only a minimal role to play in its management. As a rule, drugs should be used sparingly and only when other strategies to reduce maladaptive behaviours have been properly tried and have failed to bring about the desired changes. Use of drugs should remain infrequent before age 5 years, and practitioners should bear in mind the increased incidence of epilepsy in autism when employing drugs that might lower the seizure threshold.

Although there is no strong evidence of dopamine involvement in autism, neuroleptics have been used for a long time to decrease aggressivity, stereotypic behaviours, and impulsivity. Low-potency neuroleptics were soon abandoned, owing to their cognitive and sedative side effects. Among high-potency neuroleptics, haloperidol has been studied most. Several controlled studies showed benefits over

placebo among young children treated with dosages in the range of 1 to 2 mg daily to improve attention and to reduce hyperactivity, anger outbursts, and stereotypies (82–85). However, problematic side effects in the form of acute dystonic reactions, withdrawal dyskinesias, and tardive dyskinesias were noted (84,85). Classic neuroleptics have been replaced with atypical antipsychotics that combine dopamine (D_2) and serotonin (5-HT_2) receptor antagonist actions. Following several open-label studies suggesting the efficacy of risperidone, a 12-week, double-blind, placebo-controlled trial was conducted with 31 adults (mean age 28 years) with autism and PDD NOS (88). Significantly, at a mean dosage of 2.9 mg daily, more responders (57% vs 0%) were found in the risperidone than in the placebo group, and improvements were noted for irritability, anxiety or nervousness, aggression, repetitive behaviours, and depression. There were no improvements on objective measurements of social behaviour and language, suggesting that the drug targets nonspecific behavioural problems associated with autism. The drug was well tolerated. More recently, a multicentric, 8-week, double- blind, placebo-controlled trial of risperidone (dosage range 0.5 to 3.5 mg daily) was completed on 101 children with autism aged 5 to 17 years (mean age 8.8 years) presenting with clinical levels of tantrums, aggression, and self-injurious behaviour (89). Significant benefits of the active medication were observed for the 2 primary outcome measures of reduced Irritability scores (57% vs 14%) and a rating of "much improved" or "very much improved" on a Clinical Global Improvement (CGI) scale (69% vs 12%). Side effects such as fatigue, drowsiness, increased appetite, and drooling were more common in the risperidone group, as was a significantly higher weight gain (2.7 vs 0.8 kgs). Promising open-label studies have been conducted with olanzapine, quetiapine, clozapine, and ziprasidone; several randomized studies are currently under way. Atypical neuroleptics therefore appear to be promising agents to treat behavioural symptoms often occurring among autism patients. Yet, despite their good tolerance, these drugs are associated with some undesirable adverse effects, such as tachycardia in young children taking risperidone and sedation for all atypicals, the most serious of which is substantial weight gain. There are no long-term studies of the drugs' efficacy and tolerability.

One of the most robust biological findings in autism is that about 30% of cases show raised levels of whole-blood 5-HT (90). In addition, there is evidence that 5-HT brain synthesis is altered in children with autism (91). The 5-HT agonist fenfluramine was first used in autism patients. Initially optimistic results were not confirmed in controlled studies, and fenfluramine has been since abandoned in light of its severe complications. Among the tricyclic antidepressants, clomipramine, the most potent serotonin reuptake inhibitor, has been extensively studied. In a 10-week, double-blind, crossover study, clomipramine was compared with both desipramine and placebo in 24 outpatients with autism (92). Clomipramine was significantly superior to desipramine and placebo in reducing stereotypies and compulsive and ritualized behaviours, whereas desipramine and placebo did not differ. Both clomipramine and desipramine were superior to placebo in improving hyperactivity symptoms. However, as in other studies of clomipramine (93), serious side effects (that is, QT prolongation, tachycardia, seizure, urinary retention, constipation, and tremor) were observed with clomipramine. Since then, several open-label studies have examined the efficacy of selective serotonin reuptake inhibitors (SSRIs) in reducing behavioural problems in autism (94,95). In a 12-week, double-blind, placebo-controlled trial of fluvoxamine (at 50 to 300 mg daily, mean dosage 277 mg daily), 30 adults with high-functioning autism showed a significant response rate (53% vs 0%) in favour of fluvoxamine. Repetitive thoughts and behaviour, aggression, and other maladaptive behaviours decreased, and social relatedness and language use improved (96). Few side effects (that is, sedation and nausea) were reported, and the tolerance was excellent among these adults. Nevertheless, a 12-week, placebo-controlled, double-blind study of 34 children aged 5 to 18 years (mean age 9.5 years) taking fluvoxamine (mean dosage 107 mg daily) failed to document a benefit: only 1/16 subjects improved, and 14 children exhibited behavioural activation (94). This differential response by age to an SSRI requires further study. Other SSRIs, such as paroxetine, fluoxetine, and sertraline, have been used successfully in open-label studies (95). Several randomized trials are in progress, including one with citalopram. Other serotoninergic drugs such as venlafaxine, 5-HT_{2A} antagonists (that is, trazodone), or buspirone have been tried in case studies or open-label studies.

Children with autism have shown mixed response to methylphenidate or dexedrine used to treat hyperactivity, with frequent untoward side effects (that is, increased seterotypies, irritability, and sadness), especially at higher dosages. However, more recent studies have documented some benefits in terms of reduced hyperactivity (97–99). Alpha2-adrenergic agonists (that is, clonidine and guanfacine) have also been used successfully in open-label studies (100). Theories establishing a link between autism and increased levels of endorphins have led to studies of naltrexone. While results were initially positive and the drug was well tolerated, more rigorously controlled studies have shown only marginal benefits with regard to restlessness and hyperactivity and none with regard to social behaviour (101,102). Anticonvulsants have occasionally been used for their mood stabilization property to reduce affective instability and

impulsive aggression in autism, but no controlled study is available. Other drugs, such as dimethylglycine (DMG) and the anticholinesterase inhibitor donepezil, have been tried with unclear results. Interest in drugs targeting glutamate receptors has increased recently. A double-blind, placebo-controlled study of 39 children with autism, aged 5 to 19 years, taking an antiparkinsonian drug (specifically, amantadine at 5 mg/kg daily) showed a modest gain on clinician-rated, but not parental, measures (103). Finally, despite the publicity it has received in recent years, the gastrointestinal peptide secretin has consistently failed to show efficacy once tested in double-blind, placebo-controlled studies (104–107). More details about drug management can be found in recent reviews (95,108,109).

Summary

Our purpose was to provide an overview of recent research on autism that addresses 4 broad topics: early detection, intervention, education, and psychopharmacological management. Assuming that optimal outcomes will be achieved through the earliest intervention possible, research has recently focused on developing autism-specific first- and second-level screens (for population-based screening and screening of patients referred for developmental concerns, respectively). To date, however, existing evidence or the lack thereof places real limits on their clinical usefulness. The importance of such research is underscored by evidence converging on the conclusion that outcomes for children with autism can be significantly enhanced by early intensive intervention. Although many questions remain (notably, What are the critical therapeutic components? For whom? For what domains of development? For what intensity and duration?), effective interventions all target specific skills and are characterized by carefully planned, delivered, and monitored individualized teaching, regardless of orientation.

Not surprisingly, attention is increasingly focusing on how gains made in early intervention can be sustained and further developed during the school years. Most children with autism are educated within the public school system, typically in regular classes, either full- or part-time. Among the most pressing challenges are the need for more coordinated efforts among the various professionals involved, for training of school personnel in evidence-based teaching and behavioural management practices, and for greater attention to the emotional and social well-being of children with autism. Psychotropic drugs may be helpful in managing some behaviours associated with autism but should be seen as playing a minimal role in the overall treatment of affected children. We end by emphasizing that much progress has been made in understanding and treating children with autism, and all indications are that earlier detection and intervention will do much to minimize the associated disabilities even further.

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Résumé : Troubles du spectre autistique : détection précoce, intervention, éducation et traitement psychopharmacologique

Notre compréhension et notre traitement des enfants souffrant d'autisme ont changé radicalement depuis la première fois où Leo Kanner a officiellement documenté ce trouble en 1943.

En se référant au contexte historique, cet article examine la recherche récente portant sur 4 grandes questions : la détection précoce, l'intervention, l'éducation et le traitement psychopharmacologique des enfants souffrant d'autisme et de troubles du spectre (autistique) connexes (ci-après, « autisme »).

D'après notre examen des données probantes, nous concluons qu'en l'absence de données additionnelles plus convaincantes, l'utilité clinique des instruments de dépistage actuels demeure douteuse. Toutefois, l'importance potentielle de cette recherche est soulignée par les avantages nets d'une intervention comportementale précoce : malgré les différences d'orientation, les résultats des enfants souffrant d'autisme peuvent grandement s'améliorer grâce à l'intervention intensive précoce. Même si bien des questions demeurent en suspens (notamment, quelles sont les composantes thérapeutiques essentielles? pour qui? pour quels aspects du développement? à quel niveau d'intensité et quelle durée?), les interventions qui se sont révélées efficaces sont toutes soigneusement planifiées, exécutées, surveillées et conçues pour cibler des domaines de compétences spécifiques.

Intégrer les enfants souffrant d'autisme dans des classes régulières du système scolaire public pose un certain nombre de défis, dont le plus important est le grand nombre d'employés des écoles qui doivent être formés en enseignement fondé sur des données probantes et en pratiques de gestion du comportement. Enfin, les psychotropes peuvent contribuer à réduire certains symptômes, mais ils ne constituent ni une cure ni un substitut à d'autres formes de soutien et d'intervention.