



The Efficacy of Early Start Denver Model Intervention in Young Children with Autism Spectrum Disorder Within Japan: A Preliminary Study

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Objectives: Among the many intervention programs for children with autism spectrum disorder (ASD), the Early Start Denver Model (ESDM) is one of the few approaches that has succeeded in demonstrating clinical efficacy in randomized control trials. Here, we investigate the clinical efficacy of ESDM intervention in young children with ASD in a community setting within Japan.

Methods: All subjects were children with ASD who received ESDM intervention during the study period. Each ESDM session lasted 75 min and occurred once per week for at least 12 weeks. The outcome measures consisted of the Kyoto Scale of Psychological Development (K-test), Aberrant Behavior Checklist-Japanese version (ABC-J), and the Clinical Global Impression-Severity scale (CGI-S).

Results: Twenty-seven subjects (29.4 ± 6.4 months old) received ESDM intervention that lasted for 8.0 ± 2.6 months on average. The score on Language and Social developmental quotient on the K-test increased significantly after the intervention. The total scores on the ABC-J and CGI-S significantly decreased after completion of the ESDM intervention.

Conclusion: Our results suggest that ESDM intervention could reduce the severity of distinct clinical features of ASD, such as impairments in social interaction and communication assessed by the K-test, and maladaptive behavior rated by the ABC-J and CGI-S. We believe that the ESDM adapted to each institution might become one of the standard options for children with ASD in Japan.

Key Words: Autism spectrum disorder; Neurodevelopmental disorder; Early intervention; Pervasive developmental disorder; Early Start Denver Model.

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INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social interaction and communication as well as restricted, repetitive patterns of behavior, interests, or activities [1]. Over the years, the prevalence of ASD has steadily increased. The annual report by the Centers for Disease Control and Prevention (CDC) noted that approximately 1 in 54 children (1.85%) was identified as having ASD in 2019 as per the estimate made by the CDC's Autism and Developmental Disabilities Monitoring Network [2]. A large general population-based study conducted in

South Korea reported that the prevalence of ASD was estimated to be 2.64% [3]. Recently, a similar study in Japan demonstrated that the adjusted rate of ASD could be as high as 3.22% [4]. As the incidence of ASD could be much higher than earlier estimates, and since individuals with ASD require continuous medical and welfare support throughout their lives depending on the severity of their ASD features [5], effective intervention strategies for subjects with ASD at an early life stage is an urgent necessity.

Although there are several intervention programs for children with ASD, many failed to establish their effectiveness in clinical trials [6]. However, the clinical efficacy of the Early Start Denver Model (ESDM) has been underscored through a compelling randomized controlled trial (RCT) [7]. Since the publication of the report outlining the successful, mea-

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asurable outcomes of ESDM, the technique has been recognized as an effective intervention strategy for ASD patients by eminent experts across the world. In their study, Dawson et al. [7] performed interventions for toddlers with autism in an RCT design and demonstrated that ESDM could reduce the severity of ASD diagnosis as assessed by the Autism Diagnostic Observation Schedule (ADOS) [8].

ESDM is a naturalistic developmental behavior intervention that considers the toddlers' normal development in relation to adults and is based on applied behavioral analysis. ESDM is mainly administered to those between 12 and 36 months of age, although it might continue to positively affect until 48 to 60 months. ESDM intervention significantly promotes eye contact and joint attention in children with ASD and others during joint activity routine. ESDM could also improve reciprocal social interactions by using sensory, social routines. The child's communication skills might be significantly and rapidly facilitated by sharing enjoyment with an adult.

However, ESDM is usually an intensive intervention (15–25 hours per week for 24 months or more) program. Most countries, including Japan, lack adequate public financing and a medical and welfare workforce to support such a process on a large scale.

In this study, we investigated the clinical efficacy of ESDM intervention in young children with ASD in Japan by administering developmental tests and assessment tools at the beginning of and upon completing ESDM therapy delivered in an individualized setting.

METHODS

Participants

All children with ASD who received ESDM intervention at Tokiwa Child Development Center, Tokiwa Hospital between April 2018 and April 2019 were invited to participate in this study. The clinical diagnosis was confirmed by a consensus among a multi-professional team (consisting of a psychologist, occupational therapist, speech therapist, and a child psychiatrist certified in ESDM) as per the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [1]. The diagnosis was further confirmed by reference to the results of a set of developmental and psychological tests, including ADOS, Second Edition (ADOS-2) [9].

There were no exclusion criteria for this study. However, three subjects were excluded from the analysis, one each because of the incidence of encephalitis, movement to another city, and withdrawal of consent.

ESDM intervention in this study

The ESDM intervention was delivered in an individualized setting; wherein there was a therapist and a young child with ASD and their mother or another family member as an observer in a well-prepared room. Generally, ESDM intervention is implemented intensively, 15 to 25 hours per week for two years or more. However, most medical or welfare institutes cannot provide such intensive therapy in terms of financial aspects and limited human resources. In this study, each ESDM session lasted 75 minutes. The ESDM intervention was delivered by a certified therapist, the first author of this paper, or one of the other therapists under the supervision of a certified therapist, once a week. In response to the increasing need to provide ESDM therapy in community settings, the UC Davis MIND Institute published a policy statement in 2019 on its website. It encouraged more practitioners to implement ESDM intervention within their settings. These might be different from the conditions in which the original ESDM was developed. To maintain the quality of ESDM therapy, we strictly followed the curriculum standards described in the ESDM manuals. ESDM-certified therapists referred to the curriculum checklist to develop objectives. They examined the fidelity of the therapy provided by other therapists through on-site supervision or discussion over recorded materials.

Several studies have demonstrated the efficacy of a low-intensity ESDM, which provided less frequent and shorter sessions, and a shorter duration of the intervention [10-13]. The length of each session and the duration of ESDM intervention were as follows: three hours per week for 15 months by Devescovi et al. [13], five hours per week for two months by Xu et al. [11], six hours per week for six months by Colombi et al. [12], and eight hours per week for six months by Lin et al. [10]. Taken together, our ESDM intervention might be defined as a low-intensity ESDM in terms of density and length. In this study, the individual ESDM interventions were delivered for at least a 12-week period or a maximum of approximately 12 months subjects were shifted to the usual group therapy in the ordinary community settings when a therapist considered that the child was ready to move to a group. Each session included a short briefing to the observer regarding generalized concepts of ESDM and specific methods of applying the paradigm at home.

Measures

The Kyoto Scale of Psychological Development

The Kyoto Scale of Psychological Development (K-test) (Society for the Kyoto Scale of Psychological Development Test) [14,15] is a popular developmental test in Japan. The K-

test is a standardized and individualized psychological test that is administered by experienced psychologists to evaluate the developmental level of the subjects in three respective domains: Postural and Motor (P-M; fine and gross motor functions); Cognitive and Adaptive (C-A; non-verbal reasoning or visuospatial perceptions assessed using materials); and Language and Social (L-S; interpersonal relationships, socialization, and verbal abilities). The developmental quotient (DQ) was calculated by dividing the developmental age (DA) measured by scores in each area by the subject's chronological age.

A previous study reported the K-test's clinical usefulness for the cognitive assessment of children with pervasive developmental disorders, which is equivalent to the clinical definition of ASD in DSM-5 [15]. Another Japanese group compared domain DQs of the K-test with scores on each of the four regions in the Bayley Scales of Infant Development-II (BDI-II) [16], that is, cognitive, language, social, and motor. The correlation between the L-S DQ of the K-test and the language domain of the BDI-II at 18 months was high ($r=0.60$) [14]. Furthermore, unlike other developmental tests that estimate the score by comparing with a norm sample in the same age group, the K-test calculates the child's developmental level by dividing the DA obtained through the standardized assessment and scoring procedure in the test by chronological age [14]. Thus, we assessed the efficacy of the ESDM intervention using the K-test.

In general, DQ scores higher than 80 are regarded as typical developmental levels. The K-test takes approximately 20 to 40 min to complete.

Aberrant Behavior Checklist-Japanese version

The Aberrant Behavior Checklist (ABC) was developed to assess the therapeutic effects on severely mentally disabled individuals by scoring the severity of maladaptive behaviors observed in the subjects [17]. ABC consists of five factors: 1) Irritability, Agitation, Crying (15 items), 2) Lethargy, Social Withdrawal (16 items), 3) Stereotypic Behavior (7 items), 4) Hyperactivity, Noncompliance (16 items), and 5) Inappropriate Speech (4 items). The ABC is designed to be scored by the caregiver on a 4-point Likert scale ranging from 0 to 3. The reliability and validity of the Japanese version of the ABC have been reported previously [18]. The clinical usefulness of ABC for the behavioral assessment of children with ASD [19] and children under the age of 5 [20] have also been reported.

In this study, all caregivers, mostly the mothers of the subjects, were requested to rate the severity of behavioral symptoms in their children before and after the ESDM intervention.

The Clinical Global Impression-Severity scale

The Clinical Global Impression-Severity scale (CGI-S) is a simple and easy rating scale developed to evaluate the severity of clinical symptoms in targeted subjects [21]. Raters are scored on a 7-point Likert scale, where a higher score indicates a more severe condition. We used the CGI-S to rate the overall severity of ASD symptoms, behavior, and function in the past seven days. In this study, two of our team members, other than the principal therapist in charge, scored CGI-S independently, and a consensus score was expressed as CGI-S rater.

Statistical analysis

All statistical analyses were performed using StatFlex Ver.6 (Artec Inc., Osaka, Japan). For comparing two related samples (pre- vs. post-ESDM), the Wilcoxon signed-rank test was used. Statistical significance was set at $p<0.01$ (two-tailed).

Ethics

The ethics committee approved the study protocol of To-kiwa Hospital before data collection (TH-180201). Informed written consent was obtained from all the guardians before enrollment in the study. This study was conducted as per the principles of the Declaration of Helsinki.

RESULTS

The mean age of the 27 subjects was 29.4 ± 6.4 (15–40) months old at the initiation of ESDM intervention. The mean overall DQ measured by the K-test before the intervention was 77.3 ± 12.7 . On average, the intervention lasted 8.0 ± 2.6 months, with a range of 3 to 13 months. The mean K-test interval between pre- and post-intervention was 12.3 ± 2.8 months. Because all subjects completed the K-test within 3 months of initiation and less than 3 months after completing ESDM, the interval for K-tests ranged from 8 to 18 months (Table 1).

The results of the efficacy of ESDM intervention are summarized in Table 2.

The Wilcoxon signed-rank test revealed that there were no significant pre-post differences in total DQ (pre: 77.3 ± 12.7 /post: 75.4 ± 13.7), P-M DQ ($85.6\pm 14.3/82.3\pm 12.3$), or C-A DQ ($79.0\pm 14.2/78.2\pm 14.4$). However, L-S DQ after the intervention was significantly higher when compared to the time before the intervention, 64.8 ± 19.7 vs. 70.8 ± 19.0 , $p=0.0094$.

The mean total ABC-J score decreased from 44.2 ± 26.4 to 22.3 ± 13.7 . Statistical significance was found between these two scores using the Wilcoxon signed-rank test.

CGI-S scores rated by our team and caregivers changed from 4.1 ± 0.8 to 2.9 ± 0.6 and 4.5 ± 1.2 to 2.9 ± 0.9 , respectively.

Table 1. Summary of the subjects

Subjects	27
Gender	
Boy	18
Girl	9
Age (months)	29.4 ± 6.4 (15–40)
Pre-ESDM overall DQ of K-test	77.3 ± 12.7 (52–109)
ABC-J	44.2 ± 26.4 (8–122)
CGI-S rater	4.1 ± 0.8 (3–6)
CGI-S parent (s)	4.5 ± 1.2 (2–7)
Length of ESDM (m)	8.0 ± 2.6 (3–13)
Interval of K-test (m)	12.3 ± 2.8 (8–18)

The results are expressed as mean ± standard deviation. The numbers in parentheses mean the ranges. ESDM: Early Start Denver Model, DQ: developmental quotient, K-test: The Kyoto Scale of Psychological Development, ABC-J: Aberrant Behavior Checklist-Japanese version, CGI-S: Clinical Global Impression-Severity scale

Table 2. Summary of the results

	Pre-ESDM	Post-ESDM	p
ABC-J	44.2 ± 26.4	22.3 ± 13.7*	<0.001*
CGI-S rater	4.1 ± 0.8	2.9 ± 0.6*	<0.001*
CGI-S parent (s)	4.5 ± 1.2	2.9 ± 0.9*	<0.001*
K-test			
Overall DQ	77.3 ± 12.7	75.4 ± 13.7	0.197
P-M	85.6 ± 14.3	82.3 ± 12.3	0.132
C-A	79.0 ± 14.2	78.2 ± 14.4	0.420
L-S	64.8 ± 19.7	70.8 ± 19.0*	0.0094*

*Statistically significant. ESDM: Early Start Denver Model, ABC-J: The Aberrant Behavior Checklist-Japanese version, CGI-S: Clinical Global Impression-Severity scale, K-test: The Kyoto Scale of Psychological Development, DQ: developmental quotient, P-M: Postural and Motor, C-A: Cognitive and Adaptive, L-S: Language and Social

DISCUSSION

This study demonstrated that ESDM intervention integrated into a common developmental support program for young children with ASD in a community setting within Japan could reduce the severity of social impairments and language delay as assessed by the K-test, and maladaptive behaviors rated by ABC-J and CGI-S.

Deficits in social communication and social interactions are the core features of ASD. Our results suggest that ESDM intervention utilizing our protocol (75 minutes per session and once per week) could reduce the severity of certain clinical symptoms of ASD, such as poor eye contact or impairment in social interaction, as assessed by the K-test. The slight decrease in the overall DQ of the K-test (77.3 ± 12.7% vs. 75.4 ± 13.7%) might be attributed to the delayed development in the Postural-Motor and Cognitive-Adaptive domains com-

pared to the children without ASD because the overall DQ is calculated from the estimated DA through various tasks of the K-test divided by the chronological age.

Accumulating evidence suggests that ESDM intervention almost certainly alleviates social interaction deficits in children with ASD [22,23]. There is a serious shortfall in the medical and welfare workforce of young children with ASD in Japan [24]. It is almost impossible for us to provide intensive ESDM interventions to all the referred cases of ASD. Thus, those working in this field are caught in the dilemma of being unable to provide enough therapies to young children with ASD who have the possibility of improving their social skills by receiving ESDM intervention. The present study results suggest that ESDM intervention, which is modified to be practically feasible in our common clinical settings, could help in alleviate deficits in social communication and interaction in children with ASD.

In Japan, there is a general health check-up at 18 and 36 months of age [25]. Annual statistical data by the Japanese Ministry of Health, Labor, and Welfare reports that more than 95% of all Japanese children at these ages are assessed in terms of their developmental levels at local public health centers every year. If additional research supports the efficacy of ESDM in community settings, it might be very effective to initiate it in children with ASD soon after the 18-month health check-up, integrated into the public health system as is done in some European countries [12,26].

Maladaptive behavior is prevalent in children with ASD [27]. It is common for young children with ASD to have self-injurious, aggressive, disruptive, and destructive behaviors. In this study, we scored the severity of maladaptive behaviors using the ABC-J. As a result, the mean total ABC-J score rated by their mother or another family member decreased from 44.2 ± 26.4 (pre-ESDM) to 22.3 ± 13.7 (post-ESDM). Previous studies have demonstrated a close relationship between impairments in social interaction and the prevalence of maladaptive behavior in young children with ASD [28]. Our results were consistent with these findings concerning the decreased severity of maladaptive behaviors on ABC-J that was related to the improvement in social interaction as assessed by the K-test. In general, maladaptive behaviors observed in children with ASD remain or worsen without appropriate intervention. Furthermore, specialized therapies for ASD require more expenses than other developmental disorders, especially when they have comorbid behavioral problems [29]. Maladaptive behaviors could be the most serious problems that hinder children with ASD from being included in group settings such as group therapies, daycare services, or preschools. Thus, early intervention for behavioral problems in children with ASD is essential.

The CGI-S scores rated by our team and caregivers, majorly their mothers, decreased from 4.1 ± 0.8 to 2.9 ± 0.6 and 4.5 ± 1.2 to 2.9 ± 0.9 (pre- vs. post-ESDM), respectively. These results suggest that caregivers were aware of the significant alleviation of various clinical symptoms related to ASD features in their children. It has been reported that the level of psychological distress among caregivers of children with ASD is associated with the severity of behavioral problems and clinical symptoms of ASD in their children [30]. Minimizing the concerns and anxieties of these individuals is an essential component of therapeutic interventions. To this end, the earlier the ESDM intervention begins, the more effective it becomes in improving the quality of their and the affected children.

This study has several limitations, such as the small sample size and pre-post design without controls. Replication with a larger sample, in a randomized controlled design, and additional measures, such as ADOS-2, are necessary. However, to the best of our knowledge, this is the first study in Japan to demonstrate the efficacy of ESDM intervention in young children with ASD.

We hope that specialized interventions such as the ESDM adapted to each institution might become one of the standard options for children with ASD and their families in Japan.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

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