Early intervention in severe Autism : positive outcome using EDT

Blanc R.^{1,2*}, Latinus M.^{1,3,4*}, Guidotti M.^{1,3}, Adrien J.L.², Roux S.³, Dansart P.¹

Barthélémy C.³, Rambault A.¹, Bonnet-Brilhault F.^{1,3#}, Malvy J.^{1,3#}.

1. Exac-T, Centre Universitaire de Pédiopsychiatrie, CHRU de Tours, Tours, France
2. Université de Paris, Laboratoire de Psychopathologie et Processus de Santé, F-92100 Boulogne Billancourt, France.
3. UMR 1253, iBrain, Université de Tours, INSERM, Tours, France
4. Centro de Estudios en Neurociencia Humana y Neuropsicología. Facultad de Psicología. Universidad Diego Portales, Santiago, Chile

* joint first authors

joint last authors

Correspondence:

[Romuald Blanc](#)

romuald.blanc@u-paris.fr ; r.blanc@chu-tours.fr

Abstract:

Early intervention programs positively affect key behaviours for children with Autism Spectrum Disorder. Yet, most of these programs do not target children with severe autistic symptomatology associated with intellectual disability (ID).

The aim of this study was to investigate psychological and clinical outcomes of children with severe autism and ID enrolled in the **Tailored and Inclusive Program for Autism - Tours** (TIPA-T). The first step of the TIPA-T is the Exchange and Development Therapy (EDT): an individual neurofunctional intervention, consisting of one-to-one exchanges between a child and a therapist taking place in a pared-down environment. It aims to rehabilitate psychophysiological abilities at the roots of social communication, through structured sequences of “social play”.

Cognitive and socio-emotional skills and general development were evaluated with the Social Cognitive Evaluation Battery (SCEB) scale and the Brunet-Lézine scale-Revised, respectively, before and after 9 months of intervention in 32 children with ASD and ID. Autistic symptomatology was evaluated with the Behavior Summarized Evaluation-Revised (BSE-R) scale at 5 time-points in a subset of 14 children, both in individual and group settings.

Statistically significant post-intervention improvements were found in cognitive and socio-emotional skills. All but one child showed improvements in at least one social domains, and 78% of children gained one-level in at least 4 social domains. 29 children improved in cognitive domains with 66% of children improving in at least 3 cognitive domains. Autistic symptomatology evaluated in one-to-one settings significantly decreased with therapy; this reduction was observed in more than 85% of children. In group settings, autistic symptomatology also decreased in more than 60% of children. Global developmental age significantly increased by 3.8 months.

The TIPA-T, including EDT in particular, improves socio-emotional skills of most children with ASD and reduces autistic symptomatology; yet, with heterogeneous outcomes profiles, in line with the strong heterogeneity of profiles observed in ASD. At the group level, this study highlights the benefits of the TIPA-T for children with severe autism and associated ID. Assessment of autistic core symptoms showed an improvement of social interaction, both in one-to-one and group evaluations, demonstrating the generalizability of the skills learned during the EDT.

Key-words: Autism Spectrum Disorder, Children, Assessment, Exchange and Development Therapy, Tailored and Inclusive Program for Autism - Tours.

Abbreviations : ASD : Autism Spectrum disorder ; TIPA-T: Tailored and Inclusive Program for Autism - Tours; EDT : Exchange and Development Therapy, SCEB : Socio-emotional and Cognitive Evaluation Battery, BSE-R : Behavioural Scale Evaluation-Revised

Introduction

As defined in the DSM-5 (1), autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social communication and social interaction and by restricted, repetitive patterns of behavior, interest, or activities that manifest during the first years of life. ASD is frequently associated with intellectual disability (ID, 2), with lower intellectual quotient linked to more severe autism symptoms (3). Most individuals with ASD and/or ID require some level of lifelong support because of the severity of these conditions and the high prevalence of related comorbidities. In addition, ASD is also characterized by an important heterogeneity, notably regarding the severity of autism but also at all level of clinical examination: biological, genetic, cognitive, neural and behavioural (e.g., 4, 5). Early intervention programs positively affect key behaviours for children with ASD. Yet, most of these programs do not target children with severe autistic symptomatology associated with intellectual disability. The aim of this study was to investigate psychological and clinical outcomes of children with severe autism and intellectual disability enrolled in the Early Phase of the **Tailored and Inclusive Program for Autism - Tours** (TIPA-T).

Early intervention for children with Autism Spectrum Disorder has been recognized as a health and educational priority (6, 7). Early (i.e., starting before 4 years old) intensive behavioural interventions are recognized as an efficacious approach for improving outcomes for young children with ASD (8-12). Well-known intervention programs based on a naturalistic developmental behavioural approach include the Early Start Denver Model (13), the Joint Attention Symbolic Play Engagement and Regulation (JASPER – 14, 15), pivotal Response Treatment (PRT – 16, 17, 18), Paediatric Autism Communication Therapy - Generalised (PACT-G – 19), The Frankfurt early intervention program (FFIP – 20, 21).

Existing intervention program mostly targets children with no or mild intellectual deficiency. The **Tailored and Inclusive Program for Autism - Tours** (TIPA-T) program evaluated in the current study is dedicated to all children, from toddlers to young adults, including those with severe autism and associated intellectual disability.

The TIPA-T is a tailored and global program based on functional, developmental, and multidisciplinary assessments of the children. The program is set up by a multidisciplinary team, which includes psychiatrists, psychologists, speech therapists, psycho-motor therapists, social workers, teachers and nurses located in the child psychiatry intervention units in the Center of Excellence for Autism in Tours (Exac-T, France). The program is tailored to each child's age and needs following an integrative

approach to the treatment of ASD and includes both individual and collective sessions. The current paper focuses on the early phase of TIPA-T, dedicated to children between 2 and 6 years old. The weekly program duration is 20 to 25 hours following the recommendations of the High Authority for Health in France (HAS, 2012) integrating individual and collective care times (Exchange and Development Therapy – EDT, speech therapy, psychomotor therapy, educative activities) and school sessions in mainstream kindergarten with individualized support.

Collective interventions, spread on the whole day, comprise speech and psychomotor activities performed by trained professionals, an educative program proposed by nurses and specialized teachers within the child psychiatric unit, alongside group free play aiming at working on socialization, communication, and autonomy. Collective interventions also integrate inclusive school sessions with individual support.

Individual intervention mainly consists of sessions of Exchange and Development Therapy (EDT), an individual neurofunctional therapy based on the experience and practice of a multidisciplinary team (22-24). The EDT aims at re-educating psychophysiological abilities at the roots of social communication, which will in turn improve behavior, rather than targeting behavior first. It focuses on developing, increasing, and enriching social contacts and exchanges with others through adapted means of communication. It is based on the underlying assumption that autistic symptoms are the consequences of the atypical development (25-29) and malfunctioning (25, 30-37) of the cerebral networks underlying change detection and social communication. The neurophysiological principles underlying EDT are cerebral plasticity, physiological curiosity, and free acquisition. It aims to rehabilitate, through structured sequences of "social play" and shared enjoyment, functions subtended by the brain systems of social communication: attention to others, intention, imitation, etc. The EDT consists in one-to-one exchange between a child and a therapist taking place in a pared-down environment to facilitate mutual adjustments and socio-emotional synchronization between the child and the adult. This rehabilitation therapy is particularly indicated for young children before the age of 4, a period of maximum brain plasticity. The EDT is the pivotal element of the therapeutic and educational project built for a child in close relation with their family. Treatment organization is defined at the beginning of the session according to clinical and psychological assessments and to behavioural deficits. Activities tailored to each child's needs and interests, evaluated prior to the therapy, and readjusted according to longitudinal evaluations, are selected

among a list of predefined activities (e.g., bubbles, motor games, mimed song etc.). The implementation of the EDT is highly structured by visual cues, visually-based schedules, and the implementation of routines. EDT sessions takes place two or three times a week and lasts about 20 min.

A growing body of evidence on early interventions for children with ASD highlights a large variability in children's response to treatment (e.g. 38). Yet, so far, it is difficult to identify which children respond to which treatment making it difficult to recommend the intervention better suited to a specific child. Difficulty in assessing outcomes of intervention programs arose from the lack of clinical tools that provides a precise and detailed functional profile of children with autism, specifically oriented towards key symptoms of ASD and sensitive enough to assess subtle changes occurring over a very short period of time (38). In the current study, we used the Social Cognitive Evaluation Battery (SCEB; 39, 40-42), a French clinical tool created to assess young children with ASD with autism and associated ID. It explores different functional skills covering cognitive and socio-emotional domains for children with a developmental age comprised between 4 and 24 months. Complementary to the SCEB, the Behavioural Scale Evaluation-Revised (BSE-R; 32, 43) evaluates the behavior of children with autism to further assess the severity of autism. Briefly, the BSE-R focuses on several neurophysiological functions, which are believed to contribute to core symptoms of autism in varying degrees (e.g., attention, perception, association, intention, imitation, contact, communication...). The BSE-R provides a behavioral and functional profile of a child and can be used regularly to follow the evolution of a child's particular deficit (24, 32).

The aim of this study was to describe the evolution of key autistic symptoms and behaviors in some children with severe ASD and concurrent ID following a 9-months early intensive intervention program, the **Tailored and Inclusive Program for Autism - Tours** (TIPA-T) centered on the EDT. We hypothesized that the TIPA-T will yield progress in socio-emotional skills assessed with the SCEB and a reduction of autistic behaviors with the BSE-R.

Methods

Subjects

The sample consisted of 32 children (26 males and 6 females) with a diagnosis of Autism Spectrum Disorder, according to ICD 10 (World Health Organization, 1993) and DSM-5 (1) made by the multidisciplinary team of the Excellence Center for Autism - Tours (EXAC-T) after full clinical assessment. Mean chronological age was $45 \pm$ (standard error of mean – sem) 8.1 months (range in months [27 60]). All children had severe autism (Childhood Autism Rating Scale (44); mean $\pm$ sem: 38.4 ± 0.51 , [33.5 47]) and moderate-to-severe intellectual disability (Psychomotor Developmental Scale of Brunet-Lézine-Revised (45); Developmental Quotient (DQ): mean $\pm$ sem: 39.3 ± 1.8 , [15 60]; Developmental Age (DA): 17.3 ± 0.7 , [7 24]).

Scoring

The Brunet-Lézine scale-Revised (45) is an adaptation of the Gesell's scales (46), validated in the French population. It allows the evaluation of the psychomotor development of children from 1 month to 30 months of age. The Brunet-Lézine-revised allows the assessment of developmental ages in 4 different areas: posture (PDA), oculo-manual coordination (CDA), language (LDA), and sociability (SDA), as well as a global developmental age (GDA).

Cognitive and socio-emotional skills were assessed with the Social Cognitive Evaluation Battery, SCEB (40-42). Based on Piaget's, Bruner's and Fisher's theories of psychological development (47), the SCEB assesses both cognitive and socio-emotional areas of development at 4 developmental levels (level 1= from 4 to 8 months, level 2= from 8 to 12 months, level 3= from 12 to 18 months, level 4= from 18 to 24 months). Cognitive area comprised 7 domains: Self Image (SI_m), Symbolic Play (SP), Object-relation Schemata (Sch), Operational Causality (OC), Means-Ends (ME), Spatial Relations (SR) and Object Permanence (OP). Socio-emotional area includes 9 domains: Behavior Regulation (BR), Social Interaction (SI), Joint Attention (JA), Expressive Language (EL), Receptive Language (RL), Vocal Imitation (VI), Gestural Imitation (GI), Affective Relation (AR) and Emotional Expression (EE).

Autistic symptomatology was assessed using the BSE-R scale (32, 43). The BSE-R assesses 29 behaviors scored from 1 to 5 according to the frequency of occurrence (1 = never, 2 = sometimes, 3 = often, 4 = very often, 5 = always). These 29 behaviors can be grouped into two factors: Interaction deficits (Factor 1) and Modulation deficits (Factor 2). Here, the data of each factor were analyzed. The BSE-R scale is a recognized tool for its use in observational and intervention evaluation studies (48).

Organization of assessments

Scorings of the Brunet-Lezine scale and of the SCEB were performed at the beginning of therapy and after 9 months by psychologists experienced with these tools. The initial evaluation, necessary to work out a tailored therapy program constitutes the baseline. The BSE-R scale were evaluated both in one-to-one therapy session, through recordings of EDT sessions, and in collective settings to study generalization of acquired skills at months 1, 3, 5, 7 and 9 of therapy.

Data analysis

Statistical analysis and figures were made with R (version 4.0.2; 49) within Rstudio (version 1.3.1056; 50) environment using the following packages: lmerTest (51), rstatix (52), ggplot2 (53), tidyverse (54), readr (55), readxl (56), ggpubr (57), ggiraphExtra (58) and ggradar (59).

SCEB scores averaged across all social and all non-social domains (Figure 1A) were analyzed with a 2-ways repeated measure ANOVA with Time (Before/After Therapy) and Domains (Socio-emotional/Cognitive) as a within-subject factors. Previous to the ANOVA, assumptions were verified, and one extreme outlier was identified and removed from the data (Figure 2; participant 28). Shapiro-wilk tests performed on each factor combination from the 31 remaining participants highlights that the data did not differ from a normal distribution ($p > 0.09$).

For each factor of the BSE-R, longitudinal scores were fitted with a linear mixed model with two fixed-effects parameters, intercept and slope, of the linear trend over Time (e.g., month of therapy) for the population and two random effects for each subject. Random effects for a particular subject were the deviations in intercept and slope of that subject's time trend from the population. The model allowed for correlation of random effects for the same subject due to the relationship between intercept and slope (figure 3). The model was fit as: $\text{Scores} \sim 1 + \text{Time} + (1 + \text{Time} \mid \text{Subject})$. T-tests for fixed effects parameters use the Satterthwaite's method for degree of freedom calculation as in lmerTest (51).

Developmental assessments using Brunet-Lézine data were analyzed at the beginning and at the end of therapy. Global developmental age was analyzed by means of a paired student T-test after removing one extreme outlier; effect size was computed as Cohen's d. Developmental ages for each area were analyzed with Wilcoxon signed ranked test on paired data. One extreme outlier was removed for SDA analysis.

Results

Cognitive and socio-emotional assessment

A repeated measure ANOVA with Time and Domain as within-subject factor revealed main effects of Time ($F(1,30) = 125.89$, $p < 0.001$, $\eta^2[g] = 0.32$) and Domains ($F(1,30) = 97.18$, $p < 0.001$, $\eta^2[g] = 0.26$) on the average levels of the SCEB, but no interaction ($F(1,30) = 0.85$, $p = 0.36$, $\eta^2[g] < 0.001$; Figure XA). Average levels were higher for cognitive than socio-emotional domains and were higher after 9-months of therapy.

At the beginning of therapy, developmental level was low for both socio-emotional (mean level across the different domains: 1.94 ± 0.06 ; [1.2 2.8]) and cognitive domains (2.44 ± 0.09 ; [1.1 3.6]). After 9 months of therapy, mean levels had increased by about .5 for both social (2.53 ± 0.08 ; [1.7 3.4]) and cognitive (2.97 ± 0.09 ; [1.4 3.9]) domains (Figure 1A). To have a more precise comprehension of the evolution of children's profiles with therapy, descriptive statistics using statistical mode were used (Figure 1B). The statistical mode, corresponding to the level shown by most children, increased by one level with therapy for all cognitive domains but Operational Causality. For skills in the social domains, a 1-level increment was observed for Behavioral Regulation, Social Interaction, Joint Attention, Receptive Language, Vocal Imitation and Affective Relation.

Fig. 1: Cognitive and socio-emotional assessment. A. Average level across all cognitive and all socio-emotional domains before and after 9 months of therapy. Each individual is plotted as a grey line. Black dots represent group mean ± standard error of mean. B.

Radar plot of the statistical mode for each domain assessed with the SCEB. Socio-emotional are presented on the left and cognitive domains on the right of the image. Grey line: before therapy; black line: after therapy. **Socio-emotional domains:** BR: Behavior Regulation; SI: Social Interaction; JA: Joint Attention; EL: Expressive language; RL: Receptive Language; VI: Vocal imitation; GI: Gestural Imitation; AR: Affective Relation; EE: Emotional Expression. **Cognitive domains:** SIm: Self Image; SP: Symbolic Play; Sch: Object-relation Schemata; OC: Operational Causality; ME: Means-Ends; SR: Spatial Relations; OP: Object Permanence.

Exploration of individual data (Figure 2) revealed a majority of children gained at least 1-level in all the socio-emotional domains: Behavioral Regulation, Social Interaction, Joint Attention, Receptive language, Vocal Imitation, Affective Relation and Emotional Expression (Figure 2). In terms of cognitive domains, a majority of children improved in Self-image, Symbolic play, spatial relation and object permanence.

All but one child showed improvements in at least one social domains, and 78% of children gained one-level in at least 4 social domains. 29 children improved in cognitive domains with 66% of children improving in at least 3 cognitive domains.

Fig. 2: Individual data (N = 32) for the cognitive and socio-emotional assessment. Each radar plot represents a child enrolled in TIPA-T. Grey line: before therapy; black line:

after therapy. Note that Subject 28 (before last line, middle column) was an extreme outlier and was removed from the statistical analysis. **Socio-emotional domains** (on the left): BR: Behavior Regulation; SI: Social Interaction; JA: Joint Attention; EL: Expressive language; RL: Receptive Language; VI: Vocal imitation; GI: Gestural Imitation; AR: Affective Relation; EE: Emotional Expression. **Cognitive domains** (on the right): SI_m: Self Image; SP: Symbolic Play; Sch: Object-relation Schemata; OC: Operational Causality; ME: Means-Ends; SR: Spatial Relations; OP: Object Permanence).

Behavioral assessment

Fig. 3: Evolution of Factor 1 and Factor 2 of the BSE-R during therapy. A, B, C. Evaluation performed after one-to-one exchanges. D, E, F. Evaluation performed in group therapy. A, D. Average (black) and individual (grey; N= 14) scores assessed at month 1, 3, 5, 7 and 9 of therapy. B, E. Correlation of within-subjects random intercept and slopes for factor 1 in individual and group therapy session respectively. C, F.

Correlation of within-subjects random intercept and slopes for factor 2 in individual and group therapy session respectively.

Exploration of the interaction and modulation deficits assessed with the BSE-R in individual EDT session revealed an average reduction of symptoms of 0.92 and 0.88 respectively. Attenuation of interaction deficits were observed in 93% of children and modulation deficits decreased in 86% of children.

For the interaction deficits factor, estimated fixed parameters (β) for Time, across the population, were significant for both intercept (β [95%CI]: 3.6 [3.3 3.9]; $T(14) = 22.3$; $p < 0.0001$) and slope. (β [95%CI]: -0.11 [-0.15 -0.07]; $T(14) = -5.8$; $p < 0.0001$), highlighting that interaction deficits before therapy were high but decreased by about 0.1 point (on a 5-point scale) per month of therapy (Figure 3A). Standard deviation of random effects for intercept and slope were 0.54 and 0.05 respectively, suggesting that in a typical population expected Factor 1 scores would vary between 2.55 and 4.65 and that the expected decrease due to therapy would vary between -0.2 et -0.002. In addition, a high within-subject correlation between random effects for intercept and slope (-0.87; Figure 3B) for factor 1 was observed highlighting a strong relationship between severity of interaction deficits at the start of therapy and decrease in autistic symptomatology in the population: the larger the deficits at the start of therapy, the larger was the improvement brought on by the therapy.

For the modulation deficits, estimated fixed parameters for Time were significant for intercept (β [95%CI]: 2.3 [2.1 2.6]; $T(14) = 20.2$; $p < 0.0001$) and for slope (β [95%CI]: -0.1 [-0.15 -0.06]; $T(14) = -4.95$; $p = 0.0002$; Figure 3A), revealing that typical modulation deficits (F2) in the population were less high than interaction deficits at the start of therapy (2.3) but still decreased by about 0.1 point per month of therapy. Standard deviation of random effects for intercept and slope were 0.21 and 0.04 respectively, suggesting that in a typical population expected Factor 2 scores would vary between 1.92 and 2.75 and that the expected decrease due to therapy would vary between -0.18 and -0.03; random effects for slope and intercept were less correlated (correlation coefficient: -0.45; Figure 3C).

Exploration of the interaction and modulation deficits assessed with the BSE-R in group sessions revealed an average reduction of symptoms of 0.42 and 0.31 respectively. Attenuation of interaction deficits were observed in 86% of children and modulation deficits decreased in 64% of children.

For BSE-R evaluated in group therapy, effect of time was significant for both intercept (β [95%CI]: 4.1 [3.8 4.3]; $T(14) = 37.2$; $p < 0.0001$) and slope (β [95%CI]: -0.04 [-0.07 - 0.01]; $T(14) = -3.3$; $p = 0.0057$) for Factor 1 (Figure 3D), highlighting a decrease of interaction deficits of about 0.04 per month of therapy. Correlation coefficient for within-subjects' random effects of intercept and slope was -0.19 (Figure 3E). Effect of Time for Factor 2 (Figure 3D) evaluated in group therapy sessions was significant for intercept (β [95%CI]: 3.2 [2.7 3.7]; $T(14) = 12.8$; $p < 0.0001$) but not for slope (β [95%CI]: -0.05 [-0.1 0.003]; $T(14) = -1.98$; $p = 0.07$). Correlation coefficient for within-subjects' random effects of intercept and slope was high (-0.98; Figure 3F).

Developmental assessment

Global developmental age assessed with the Brunet-Lézine scale significantly increased by 3.8 months with therapy (GDA, $T(30) = 10.15$, $p < 0.001$, Cohen's $d = 1.5$; Figure 4A). On the 32 children included in the study only one child showed no increase in their global developmental age.

An improvement of about 3 months was also found in each area assessed with the Brunet-Lézine with large effect sizes ($r > 0.7$): postural developmental age (PDA, $V = 210$, $p < 0.001$, $n = 32$, $r = 0.77$; Figure 4B), oculo-manual developmental age (CDA, $V = 465$, $p < 0.001$, $n = 32$, $r = 0.87$; Figure 4C), language developmental age (LDA, $V = 300$, $p < 0.001$, $n = 32$, $r = 0.82$; Figure 4D), and sociability developmental age (SDA, $V = 465$, $p < 0.001$, $n = 31$, $r = 0.87$; Figure 4E). A large majority of children show an improvement of their developmental age over the 9-month of therapy in each area, with the smallest proportion observed for the postural developmental age (62.5% of children).

Fig. 4: Evolution developmental age assessed with Brunet-Lézine before and after 9 months of therapy. A. Global Developmental Age (GDA). B. Postural Developmental Age (PDA). C. Oculo-manual Coordination developmental Age (CDA). D. Language developmental age (LDA). E. Sociability developmental age. Black dot and error bar represent mean and sem. Grey dot and connecting lines represent individual data.

Discussion

Using clinical tools tailored for Autism Spectrum Disorder and sensible to subtle changes occurring over a short amount of time (the SCEB, and the BSE-R), positive outcomes were observed in children with severe ASD and concurrent ID following a 9-months early intensive intervention program, the **Tailored and Inclusive Program for Autism - Tours** (TIPA-T) in a specialized medical center, centered on the EDT. The TIPA-T, including its pivotal first step, the EDT, allowed for a general improvement for both cognitive and socio-emotional domains as well as a reduction in the severity of autistic symptomatology. In addition, assessment of autistic core symptoms with the BSE-R showed a decreased of interaction deficits in particular both in one-to-one and in group evaluation. The latter demonstrates the generalizability of the skills specially learned during the EDT.

Children's developmental trajectories were positive, but their evolution was atypical and characterized by uneven progress. Large individual variations in outcomes were observed in this study, which is consistent with the findings from previous research (10, 20, 21, 24, 60) and in line with the strong heterogeneity of profiles observed in ASD.

However, general improvement for each cognitive and socio-emotional domain was seen during therapy (e.g., Joint attention, imitation, social interaction...). Moreover, autistic behaviours tended to decrease (reduction in the degree of severity of the deficits in interaction and modulation), in particular in one-to-one exchange. Although we cannot be certain that these results do not reflect natural maturation of children, we believe this is unlikely because we observed progress in key domains of the autistic symptomatology, specifically-targeted by the EDT. Moreover, poor outcomes were observed in some children suggesting that natural maturation alone is unlikely to improve performance. Finally, in the current study, no children showed a worsening of their condition within the 9 months of the therapy, while a 9% worsening rate could have been expected based on natural maturation only (61).

Results of this study are consistent with other follow-up studies showing that early and intensive intervention program over a relatively short period of time yields positive outcomes for children with autism. Dawson and collaborators (13) showed the efficacy of an intensive intervention program designed for toddlers with ASD as young as 18 months of age: the Early Start Denver Model (ESDM). After 2 years of intervention, children provided with the ESDM showed significant improvements in IQ, adaptive behavior, and diagnostic status. More recently, it was shown that low-intensity ESDM is of some benefit to children with ASD in terms of imitation, engagement, and intentional vocalizations (62). The results of a 1-year study on a developmentally-based social pragmatic approach, the Frankfurt Early Intervention program FFIP, which starts on average at 66 months, showed improvements in autistic symptoms and cognitive development (20, 21). PRT, in children aged 64 months on average, results in increases in self-initiations and has positive effects on interaction and verbal communication, play skills and maladaptive behavior for a number of children (17, 18). In line with these studies, developmental and behavioural progress of children included in the TIPA-T program, which are generally more retarded, were important on a short period of time. Although the current study measures improvements following EDT in slightly older children than the ESDM, the EDT is also designed for younger children and children with ASD and severe ID, and the program can be started before age 2. The EDT relies on a functional base line which, not only allows characterizing the changes brought on by the therapy, but also help to target and prioritize specific functions, making it an essential therapeutic tool for severe children with ASD and with specific needs. Consistently, the EDT benefits more to children with severe autistic symptomatology for

whom the progression was larger. Taking together these studies demonstrate that when therapy is provided systematically for children with ASD within the framework of a highly structured and intensive therapy, behaviors contact, exchange and communication deficits are reduced both in the short- and the long-term (23, 31, 63-67). Improvements also affects both "primary" behavioural disturbances such as disorders of perception and association and "secondary" symptoms such as social withdrawal (22).

Difficulties in assessing the benefits of intervention program arose from the lack of clinical tools dedicated to assess subtle changes occurring over small period of time (38). Here, we used the Social Cognitive Evaluation Battery (SCEB 39, 40-42) which allow assessing a range of cognitive and socio-emotional skills for young children with ASD associated to a moderate-to-severe intellectual disability. The Behavioral Scale Evaluation-Revised (32, 43) provides additional information regarding the severity of autistic symptomatology focusing on key behaviors contributing to core symptoms of ASD in varying degrees (e.g. attention, perception, association, intention, imitation, contact, communication...). The use of these scales, that allows measurement of subtle changes, revealed progress in different cognitive and socio-emotional domains and a reduction in autistic symptomatology, even over a period of as short as nine months. Moreover, the BSE-R can be evaluated in one-to-one but also in group sessions allowing the demonstration of generalization of the skills learned during the EDT in particular regarding interaction deficits. Finally, using these scales helped identify the functions that were the first to respond to therapy and the ones that were resistant, providing orientations for therapy prevention and early intervention (11, 20, 24, 35). Combining autistic behaviors, cognitive and socio-emotional abilities assessments provide the basis for a richer dialogue with families to improve educational and therapeutic synergy around the child. It also meets specific needs, to specify and individualize the contents of psycho-educational and therapeutic actions making them essential batteries for child psychiatric team in daily practice.

Using these assessments complemented the findings obtained with a classical tool such as the Brunet-Lézine-R scale. Results of the Brunet-Lézine-R scale showed a general improvement in developmental age, as well as domain-specific improvement. On average the 9-months therapy yielded a 3-months gain in developmental age, and importantly this increase in developmental age was observed in a large majority of children. This highlights the benefit of the TIPA-T including specifically the EDT for the cognitive development of children considering that children with low IQ tends to maintain

their IQ over time (61), consistent with previous observations that intellectual disability in children with ASD who have benefited from early intensive care can be improved (9, 13, 68, 69). Yet, the Brunet-Lezine scale is a non-specific clinical tool which, despite allowing only for assessing the evolution of developmental ages (DA) and quotients (DQ), can be used to monitor children with ASD. The results of the current study showed that with more specialized and precise tools such as the SCEB and BSE-R, the child can be understood as a whole, and clinicians can obtain subtler and more precise information regarding the effects of treatment in children with ASD (38).

There are several important clinical implications for these data. When diagnosing young children with ASD, it is important to assess cognitive skills and social-reciprocal interaction deficits and abilities, in using standardized tests. Both measures are strongly related to outcomes and are correlated with each other. These measures can help clinicians to assess responsiveness to intervention and with treatment planning. In addition, early social-interaction abilities may be a pivotal skill that should be addressed in intervention programs. The study also emphasizes the effectiveness of intervention in very early age across autistic symptomatology severity range. A therapy such as the EDT might also benefit from being developed in at-home settings by providing support and teach parents the functional basis and the implementation of EDT at home.

Conclusions

The **Tailored and Inclusive Program for Autism – Tours including specifically EDT**, improves cognitive and social skills but also core symptoms of autism of most children with severe ASD and associated ID. Assessment of autistic core symptoms with the BSE-R showed a decreased of interaction disorder in particular, both in one-to-one and group evaluation. Importantly, this demonstrates the generalizability of the skills learned during the EDT. Yet, as for other intervention programs in autism, large individual variations were seen in the outcomes, in line with the strong heterogeneity of profiles observed in ASD. Data acquired in the current study do not allow understanding the reasons for the therapy being extremely successful in some children and less in others. Future studies should aim at identifying predictive factors of success to potentiate positive outcomes.

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