Autism - Open Access

**Research Article** **Open Access**

# T.U.L.I.P. Protocol (TCE, UOI, Leiter-R as Indicators of Predictivity) for the Assessment of the Developmental Potential in Children with Autism Spectrum Disorders

Magda Di Renzo[1*], Federico Bianchi di Castelbianco[1], Elena Vanadia[1], Massimiliano Petrillo[1], Lidia Racinaro[1] and Monica Rea[1,2]

[1]Institute of Ortofonologia (IdO), Via Salaria 30, 00198, Rome, Italy
[2]Dynamic and Clinical Psychology Department, Sapienza University of Rome, Via degli Apuli 1, 00185, Rome, Italy

## Abstract

The article aims to highlight some predictive indicators of improvement in ADOS scores in a group of 49 children with Autism Spectrum Disorders.

For this purpose we created a specific protocol named T.U.L.I.P. that, using the Fluid Reasoning of the Leiter-R, the presence of Emotional Contagion (TCE) and the ability to understand the intentions of the others (UOI) as predictive indicators, can identify a category of autistic children who positively respond to treatment and improves the autistic symptomatology.

The children who at the intake had predictive indicators of Emerging or Present UOI and TCE improved their autistic symptomatology with therapy and some of them (those with Present indicators) positively changed their ADOS diagnosis.

In pre-school children, or in the first year of their schooling, the assessment of cognitive and social components shows that relational skills have a greater importance in predicting the decrease of the ADOS scores.

The presence of predictive indicators, especially on the emotional response and the ability to understand the intentions of the others, also helps to work through a developmental- relational approach that activates in children their existing potentialities to get improvements even in the cognitive functioning. The Social Affection component of the Ados correlates with predictive indicators and accounts for an intervention targeted to the emotional dimension.

**Keywords:** Autism spectrum disorder; Emotional contagion; Understanding of intention; Leiter; Assessment

## Introduction

The Autism Spectrum Disorders were included in the DSM-5 [1] within the chapter of the neurodevelopmental disorders, that is a "group of conditions, with onset in the development period, which typically manifest in the early stages of development and are characterized by developmental deficits that produce impairments in personal, social, academic, or occupational functioning".

The dimensional approach in diagnostic classification supports the variability of the characteristics of these disorders, for the definition of which was in fact indicated in the DSM-5 the use of specifiers of gravity relative to the autistic symptoms, to the intellectual disability, to the impairment of speech and to the association with known medical or genetic conditions or environmental factors.

In children, especially preschoolers, many variables affect the structuring of autistic-like behaviors and may be crucial to their evolution [2]. Even the most recent epigenetic studies confirm these findings [3-5].

The clinical experience, the data coming from the therapeutic efficacy and the current research guidelines support the existence of "autisms", or conditions that are similar between them from the point of view of symptoms, but different in etiology and prognosis [6].

The identification of predictive indicators on the evolution of each child through the application of standardized and repeatable tools gives an important contribution in this regard, both respect to the trend of autistic symptomatology and of intellectual functioning, on the basis of a multidimensional and multidisciplinary assessment.

While, in fact, great attention has been and continues to be paid to the risk recognition and early diagnosis, which are the first and decisive element also with respect to prognosis, to date are not yet available, however, validated systems to identify criteria and/or prognostic indicators.

Our research, born from years of clinical experience and careful data analysis, would contribute to the definition of a protocol which, in addition to the diagnosis, helps to determine the prognosis providing, from the beginning, reliable indicators predictive of development, that could be monitored clinically and by specific tests and that could really individualize the therapeutic project.

Given the existence of considerable differences within the "autism spectrum" and the growing attention to the so-called vulnerability indicators in the first years of life, we think that also the therapeutic field should be individualized and differentiated.

The results of a developmental approach, based on the relationship model, especially in infancy and early childhood are now attracting

great interests. The ability to identify a category of autistic children who responds positively to a specific developmental therapeutic program, could have a high probability of promoting the development of children with autism spectrum disorder (ASD) both in socio-relational and cognitive areas. For this reason, the Institute of Ortofonologia in Rome (IdO) has implemented the T.U.L.I.P. Protocol, with active involvement of family and school, for the assessment of the developmental potential in ASD children.

Being able to estimate the developmental potential in children with autism spectrum disorders and in parallel to hold indicators related to the most suitable treatment is, in our opinion, a further conquest and a promising field of research for those who deal with this disease.

Our previous research [7] investigated the cognitive area in autistic children by evaluating the non-verbal IQ through the Leiter-R, demonstrating the effectiveness of a treatment that favors an approach based on the relationship and finding both the predictive value of Fluid Reasoning on the gradual improvement of the expression of IQ both on the decrease of the ADOS scores after four years of treatment. Data supported the hypothesis that an intervention based on the report offers a cognitive improvement regardless of the severity of autism symptomatology expressed by the ADOS score. These recent research indicates the importance and effectiveness of the first two years of this specific treatment and how the continuation of therapy in the following years not only ensure the stability of cognitive skills but also avoid any possible regressions in these areas of functioning.

In order to search for children's potentialities, albeit unexpressed, that guarantee a reliable prognostic value on the evolution of autistic symptoms, the inductive and deductive reasoning skills represent clinically relevant predictors, as expressions, independent from learning, of mental flexibility in a disorder characterized by rigid and stereotyped thinking, and so represent a potential area of expression of the social and cognitive functioning [8].

Evaluating the therapeutic efficacy of the developmental model, estimating the results over time through the re-tests, and in parallel searching for outcome predictors at the intake, needs to carefully consider another deficit area in autism, that is the ability to understand the intention of the others, which is a state of mind precursor of the theory of mind. This component is related to the level of symptoms, but especially is relevant for the significant predictive value at a prognostic level, verified after only two years of treatment, so demonstrating to be connected only to the symptomatic severity of autistic disorder and being independent from the cognitive level expressed [9].

A further possible predictor is the emotional responsiveness that children may show, assessed according to the presentations of emotional stimuli in a structured observation [10]. The lower emotional response of children with autistic symptomatology, or with greater impairment in the ability of Social Affection, corresponds to a greater presence of restricted and repetitive behaviors, finding that supports the hypothesis of the empathetic imbalance of Smith [11], for which the greater presence of such conducts would testimony defensive behaviors.

The results of the researches, in conclusion, confirm that the intellectual, relational and emotional skills, as well as the psycho-physical well-being of children with autism can be improved by a variety of non-verbal, not exclusively cognitive activities where the therapist relates to the child and his experiences and accompanies him to a more productive and less defensive state of activity and awareness.

These results support the basic assumption that in a high percentage of autistic children the primary deficit is at an emotional level even before cognitive [12] and the relational, sensorial and bodily dimensions represent the area toward which direct the therapeutic intervention.

The therapeutic experience with Autism, and the results of some recent studies allowed us to integrate issues related to both clinical practice and research, thus defining an assessment protocol that can reliably identify capabilities that are indicative of symptomatic impairment and at the same time can define a developmental trajectory for a positive evolution of the disorder and a more harmonious development of social and cognitive skills.

The working hypothesis that guided this study was to verify the reliability of the T.U.L.I.P. protocol in predicting the possible evolutions of the autistic symptoms.

## Methods

### Participants

49 preschool children diagnosed with autism (ASD) participated to this study. Of these, 39 males and 10 females, all aged between 24 and 88 months (M=44.35 ± 15.5). Most children are Italian (81.6%); an African minority (4.1%), Asian (8.2%) and Eastern Europe (6.1%). Social and cultural status of families is mostly in the average (89.8%), while only a family (2%) has a high status and 4 families (8.2%) have low status. At the time of the first assessment, these children had no phrasal language, so their cognitive level was evaluated through the nonverbal Leiter-R scale.

Children who participated in this study came in consultation at the Institute of Ortofonologia (Rome), with a diagnosis of autism and a request for treatment. To these children was confirmed the diagnosis of autism spectrum disorders according to DSM-IV criteria [13] and to the ADOS score [14] which indicates the symptoms severity. Since the research participants were recruited in 2011, at that time was not yet available nor the DSM-5, nor the Italian version of the ADOS-2, that was after introduced in 2013. The use in the re-test of the first version of the ADOS responds to the need to compare the ADOS scores obtained through the same algorithm and classification parameters, which are different in the ADOS-2 [15] and that would have made not comparable the two different versions.

The diagnostic assessment of the autistic children involved in this research has been prepared by a group of experts who have at least 10 years of experience (psychologists/psychotherapists, child neuropsychiatrists, neurologists and other specialized figures). During the treatment, which lasted four years, the children received three cognitive assessments (at the intake, after two years and after four years from the beginning of the treatment), three assessment focused on autistic symptomatology (at the intake, after two years, and after four years from the beginning of the treatment), an assessment concerning the understanding of the others' intentions and an assessment about the emotional contagion (at the intake). Clinicians who dealt with the assessments are not the same ones who are involved in therapy and clinical intervention. Children with certified neurological damage, children with sensory disabilities, children under 24 months were not included in this research. This study was carried out in accordance with the recommendations of the national guidelines and the APA ethic. Parents were required informed consent according to the Declaration of Helsinki.

### Instruments

**ADOS:** The Autism Diagnostic Observation Schedule is a standardized semi-structured evaluation procedure of the

communication and social interaction areas, including the behavioral and symbolic play assessment, which involves a series of activities that are evocative of conducts related to the autism spectrum disorder diagnosis [14]. The observation and coding of these behaviors are used to assign a score that identifies social and communication deficits of the child pertinent with autism and the autistic spectrum. The ADOS scores, included in a range that goes from 0 to 24, increase depending on the severity of autistic symptomatology, with a cut-off of 7 for the autistic spectrum and 11 for autism. Every child of the research sample had an ADOS classification from the beginning to end of the 4 years of therapy and the initial average score places the entire sample in a diagnosis of infantile autism.

**Leiter-R:** The Leiter International Performance Scale-Revised [16] is designed for the evaluation of intellectual functions of children and adolescents aged between 2 and 20 years. The Leiter-R is formulated to meet the clinical need to evaluate the non-verbal intelligence through a comprehensive analysis of the strengths and weaknesses with a view to a diagnosis that includes both neuropsychological and cognitive aspects. Nonverbal cognitive abilities do not require the capacity to perceive, manipulate and reason with words and numbers, so the scale can be administered completely without the use of verbal language, including instructions, and does not require verbal responses from the subject. The validity coefficient of the IQ score was calculated for each age group (from alpha 0.92 to 0.93). The Leiter-R has good evidence of validity from the studies on the content analysis, with data coming from an extensive analysis, from the criterion related studies, to the accuracy of classification of intellectual disability, and various studies related to the construct. The IQ scores have a mean of 100 and a standard deviation of 15. The intellectual disability is indicated by a composite score that is two standard deviations or more below the average, so that a score of 70 constitutes a borderline value.

**TCE:** The Test for the Emotional Contagion [17] allows estimating the emotional contagion, both in a quantity and quality sense, that is, the presence or absence of affective attunement in the child, through the observation of his emotional and behavioral response during the presentation of a structured stimulus (video). The child is presented 4 video recordings in which a girl with typical development expresses in nonverbal ways, the four basic emotions: happiness, sadness, fear and anger.

Each video has duration of 43 s (for 23 s the girl expresses each single emotion and for 20 s the video gets dark). For each emotion presented the observer writes on his encoding protocol the absence or presence of the expressive reproductions corresponding to the emotion stimulus and the relative bodily and behavioral responses of the child assessed.

The encoding protocol consists of five sections, four of which are graphically represented from a face on which mark the expression observed in the child for each emotion, and a check list of 16 bodily expressions that allow a quantitative analysis of the responses. The fifth section is represented by the summary of the test coding that allows a global qualitative assessment of the emotional contagion responses.

The checklist that is present in the four sections allows to identify if the child reproduces the motor pattern of the emotion observed in the girl of the video, if they participate actively, if comments verbally or vocalizes, if reproduces the intonation of emotion, if it shows postural abnormalities, if he begins to approach the observer, if he approaches

or not the video, if he starts stereotyped movements, if he ignores the video and so on.

Each response is considered as "absent" if the child does not reproduce the motor pattern of the emotion and has a score of 0; each response is considered as "present" if the child reproduces the motor pattern of the emotion and in this case the evaluation could be scored with 1, 2 or 3. It is scored with 1, that is "principle of emotional contagion", when there is one emotional contagion response and 3/4 of hints of stimulus reproduction; it is scored with 2, that is emotional "contagion", when there are from 2 to 4 emotional contagion responses; it is scored with 3, "empathy", when the child recognizes the emotions and is able to differ from his own.

Additionally, the test allows defining, through the verbalization, if the child shows veridical empathy or quasi-egocentric empathy [18]. The first assumes the differentiation between the self and the other. In the quasi-egocentric empathy, even though there is the recognition of each emotion, the process of separation between the self and the other is not still completed, so the child does not differentiate.

All the TCE evaluation procedure was videotaped and the observers scored during the observation and also confirmed it after, through the video recordings.

The measures used to evaluate the TCE, were first administered by two experienced observers who assessed independently 20 autistic children. The inter-observer reliability agreement was high (Cohen's k=0.90).

**UOI:** To assess the understanding of others' intentions, we used a modified version of the Intention condition of Behavioral Re-enactment Procedure [19]. The original version of the Meltzoff procedure involved five objects as test stimuli: the first object was a dumbbell-shaped toy that could be pulled apart and put back together again. It consisted of two 2.5 cm wooden cubes, each with a 7.5 cm length of plastic extending from it. One tubular piece fit snugly inside the other so that it took considerable force to pull them apart. The second object was a small black box (16.5 × 15 × 5.5 cm) with a slightly recessed rectangular button (3 × 2.2 cm) on the top surface. The button activated a buzzer inside the box. The box was supported by a base that tilted 30° off the table so that the front surface was facing the child. The box was accompanied by a small stick tool made of a rectangular block of wood that was used by the experimenter to push the button. The third object consisted of a horizontal prong and nylon loop. The prong was fashioned from an ornamental wooden piece with a bulbous end. It protruded horizontally from a background screen made of gray plastic (17 × 20.3 cm). The loop was made from black and yellow woven nylon tied in a circle with a diameter of 7.5 cm. The fourth object consisted of a yellow cylinder with a flared base (9.5 cm high with a 6.3 cm opening) coupled with a loop of beads (19 cm long when suspended). The fifth device was a transparent plastic square and wooden dowel. The square (10 cm) had a 2.5 cm diameter round whole cut out of the center so that if could fit over the dowel. Thin plastic strips were glued along two edges of the plastic square to raise it slightly from the table so that it could be picked up by the children. The dowel (2 cm high and 1.7 cm in diameter) was in an upright position in the center of a wooden base plate.

In the present study the procedure involved the use of only 4 items: we did not use the buzzer inside the box, because of floor effect: in a preliminary study that we carried out on a sample of 40 children with autism [20] the most part of the children with autism scored near the bottom, because the sound characteristics of the object elicited

stereotypical responses of closure: whenever this specific task was proposed, the children accentuated restricted and repetitive behaviors, which led to attentive and relational differences, as a result of which they interrupted the test. This occurred regardless of the order in which the task was proposed.

The children, in our Intention condition, look like an experimenter (E) try to unsuccessfully perform a target action (for example, E pulls apart the ends of a dumbbell, but his hands slip away); the children have never seen the target action completed and well executed and neither the object.

For each of the four items, the children are shown by E three failed attempts to perform the action. Then the object is leaved on the table in front of the child and to him is told "now, it's your turn". Once the child has touched the object, starts a time of 20 s in which the child could respond.

This procedure was then repeated with each of the remaining objects. In the Intention condition, children should understand what the E intends to do, so they should perform the action-target and not what they see him doing (for example, slide hands to the sides of the dumbbell).

Subsequently, a score from 0 to 4 is attributed on the basis of the number of tasks carried out, in reference to the four target actions. The score of 0 is assigned if there is: the inability to pay attention to the stimulus presented child; stereotyped and/or sensorial manipulation of the object; repetition of the failed attempt as seen in the experimenter; target action approximation.

The number of target action produced in the Intention conditions have been coded as follows: 0=Absence of capacity (no task performed); 1=Low capacity (1 task performed); 2=Fair capacity (2 tasks performed); 3=Good ability (3 tasks performed); 4=Excellent capacity (4 tasks performed).

All the UOI assessment procedure was videotaped and the observers scored during the observation and also confirmed it after, through the video recordings.

The measures used to evaluate the UOI, were first administered by two experts who observed independently 20 autistic children. The inter-observer agreement was high (Cohen's k=0.92).

## Data Analysis

We used the Statistical Package for Social Sciences (SPSS) version 19 for data analysis. Significance level was set at alpha 0.05 (two-tailed). Analysis of Variance (ANOVA) was used to evaluate differences between groups. Analysis of Variance for repeated measures was used to evaluate differences between groups over time. Effect sizes were reported as partial eta squared ($\eta^2_p$), A $\eta^2_p$ of 0.02 was considered a small effect size, 0.13 a medium effect size and 0.23 a large effect size. Correlation analysis was performed to analyze the relationship between dependent variables. The linear regression was conducted to verify the predictors of the severity of the autistic level.

## Aim

Goal 1: Verify the Fluid Reasoning reliability in predicting the intellectual development of children with autism and in predicting improvement in ADOS scores.

Goal 2: Verify the UOI reliability as a predictor of improvement in ADOS scores.

Goal 3: Verify the TCE reliability as s predictor of improvement in ADOS scores.

## Results

At intake, the group of 49 children with ASD was assessed with reference to autistic symptomatology (ADOS), cognitive skills (IQ and FR), ability to understand the intentions of others (UOI) and presence of emotional contagion (TCE). Table 1 describes averages and ranges of the scores.

*Goal 1: Verify the Fluid Reasoning reliability in predicting the intellectual development of children with autism and in predicting improvement in ADOS scores.*

The IQ assessment through the Leiter-R made it possible to divide the total group into 3 sub-groups: 15 children (mean chronological age 42.3 ± 9.3 months) cannot be evaluated (Not Ev. Group) because their low attention levels did not allow a structured assessment; 19 children with an IQ score between 40 and 75 (mean chronological age 45.7 ± 19.7 months); 15 children with an IQ score above 75 (mean chronological age 44.7 ± 15.3 months). The children of the three groups did not differ with respect to chronological age ($F_{2,48}=0.21$; p=0.81).

The first objective that we would verify was about the possibility for the Fluid Reasoning score to act as a Target for the IQ score. As shown in Table 2, there was a significant effect of repeated measure variable ($F_{2,48}=18.24$; p<0.01; $\eta^2_q=0.32$), so the groups improved their IQ scores over the three assessments, at the beginning, after 2 years, and after 4 years, but it is important to consider that in the Not Ev. group, even after four years, IQ score remain in the category of severe intellectual disabilities, corresponding to an IQ score<55 at the last Leiter-R assessment. In this group, the Fluid Reasoning score was stable over the years ($F_{2,14}=1.76$; p=0.14), and the IQ score has not yet reached its target score after 4 years (given by a FR of about 62). Furthermore, in this group, it is observed that the FR score remains significantly higher than the IQ score ($F_{2,14}=6.17$; p <0.01; $\eta^2_q=0.13$). Of these 15 children, 11 are not even evaluable after 2 years and 4 years.

Instead, the group with IQ>76, while showing significant IQ improvements over time ($F_{2,14}=6.20$; p<0.01; $\eta^2_q=0.16$), already started with an intellectual category in the average and remains in this category even after four years. In this group, even the Fluid Reasoning score is in the average and is already high at the first assessment and over the years it remains lower than the IQ that has reached its Target.

Finally, the group with the IQ score between 40 and 75, is the most clinically interesting group, because they are children with an important cognitive impairment but actually assessable, and with a FR significantly higher than the IQ score, at the first assessment ($F_{2,18}=30.06$; p<0.001; $\eta^2_q=0.26$). In this group, it can be observed that, not only the IQ score significantly grows over time ($F_{2,18}=19.07$; p<0.01; $\eta^2_q=0.17$), but that after 4 years the IQ score reaches its Target (given by a FR of about 74).

| | Mean ± SD | Range |
|---|---|---|
| ADOS | 16.3 (4.3) | 7-22 |
| IQ | 62.6 (18.9) | 36-102 |
| FR | 74.9 (16.8) | 48-116 |
| TCE | 1.1 (0.9) | 0-3 |
| UOI | 1.8 (1.5) | 0-4 |

ADOS: Autism Diagnostic Observation Schedule; IQ: Intelligence Quotient; FR: Fluid Reasoning; TCE: Emotional Contagion Test; UOI: Understanding of Intention Test

**Table 1:** Mean (± SD) and range of ADOS scores, IQ, FR, TCE and UOI, at intake.

| | IQ Evolution (Mean and SD) | | | | FR Evolution (Mean and SD) | | | |
|---|---|---|---|---|---|---|---|---|
| | Assessment 1 | Assessment 2 | Assessment 3 | *p* | Assessment 1 | Assessment 2 | Assessment 3 | *p* |
| All Groups | 62.9 (1.5) | 72.8 (2.7) | 76.8 (3.2) | *0.01* | 75.7 (1.6) | 75.6 (2.3) | 74.5 (2.6) | *0.60* |
| *Confidence interval 95%* | 59.9-65.9 | 67.4-78.2 | 70.3-83.3 | | 72.5-79.1 | 70.9-80.4 | 69.2-79.8 | |
| | Assessment 1 | Assessment 2 | Assessment 3 | *p* | Assessment 1 | Assessment 2 | Assessment 3 | *p* |
| Not Ev. IQ group | 46.4 (6.2) | 52.1 (19.8) | 54.1 (23.0) | *0.56* | 62.8 (6.2) | 61.3 (12.2) | 62.3 (16.9) | *0.78* |
| *Confidence interval 95%* | 41.9-50.8 | 37.9-66.3 | 37.7-70.5 | | 58.3-67.3 | 52.6-70.1 | 50.2-74.4 | |
| IQ>76 group | 87.0 (8.6) | 95.3 (14.5) | 99.5 (18.5) | *0.05* | 96.6 (11.0) | 88.2 (13.2) | 86.7 (15.0) | *0.05* |
| *Confidence interval 95%* | 81.8-92.2 | 86.6-104.1 | 88.3-110.6 | | 89.3-104.0 | 79.3-97.1 | 76.6-96.8 | |
| 40<IQ<75 group | 55.2 (11.1) | 71.1 (16.6) | 76.8 (19.6) | *0.01* | 67.9 (10.5) | 77.4 (15.6) | 74.4 (15.9) | *0.06* |
| *Confidence interval 95%* | 49.9-60.5 | 63.1-79.1 | 67.4-86.2 | | 62.8-72.9 | 69.8-84.9 | 66.7-82.1 | |

**Table 2:** Mean (SD) of IQ scores and FR scores, at first, second and third assessment.

| | ADOS Evolution (Mean and SD) | | | |
|---|---|---|---|---|
| | Assessment 1 | Assessment 2 | Assessment 3 | *p* |
| Not Ev. IQ | 18.2 (3.5) | 16.4 (3.2) | 15.5 (3.2) | 0.05 |
| *Confidence interval 95%* | 15.7-20.7 | 14.1-18.7 | 13.2-17.8 | |
| IQ>76 | 13.2 (5.0) | 8.8 (5.2) | 6.4 (4.9) | 0.01 |
| *Confidence interval 95%* | 10.1-16.2 | 5.6-11.9 | 3.4-9.4 | |
| 40<IQ<75 | 17.2 (2.8) | 13.4 (3.9) | 11.2 (5.0) | 0.01 |
| *Confidence interval 95%* | 15.8-18.5 | 11.5-15.3 | 8.7-13.6 | |

**Table 3:** Mean (SD) of ADOS scores, at first, second and third assessment, in the Not Ev. group, in the IQ>76 group and in 40<IQ<75 group.

Next, as regards the possible predictability of the FR in the change of the ADOS score, as seen in the Table 3, in the Not Ev. group a significant improvement of the ADOS score appeared after four years in ADOS category.

In the group with IQ>75 the ADOS score significantly decreases both after 2 and after 4 years ($F_{2,14}$=17.21; p<0.01; $\eta^2_q$=0.19), and the children of this group change their category switching from Autism Spectrum to No Autism.

Even in the group with the IQ score between 40 and 75 the ADOS score significantly decreases both after 2 and after 4 years ($F_{2,18}$=25.14; p<0.01; $\eta^2_q$=0.21) and the children of this group changed from an ADOS category of Autism to Autism Spectrum.

*Goal 2: Verify the UOI reliability as a predictor of improvement in ADOS scores.*

We divided the UOI scores in three categories: Absent group (N=20), Present group (N=19) and Emerging group (N=10).

In the Table 4 is shown that in children where the UOI ability is Absent at the intake, there is a significant improvement in ADOS scores in the next 2 years ($F_{2,39}$=4.98; p<0.01; $\eta^2_q$=0.20), but then this improvement will stop, and after four years the ADOS scores will remain stable (post hoc: p=0.12).

In children where the UOI ability is Emerging at the intake, there is a significant improvement in ADOS scores in the next 2 years ($F_{2,39}$=4.98; p<0.01; $\eta^2_q$=0.20), but then this improvement will stop, and after four years the ADOS scores will remain stable (post hoc: p=0.21).

In children where the UOI ability is Present there is a significant improvement in ADOS after 2 years of treatment ($F_{2,39}$=4.98; p<0.01; $\eta^2_q$=0.20), and then this improvement continue over the next two years (post hoc: p<0.01).

*Goal 3: verify the TCE reliability as a predictor of improvement in ADOS scores.*

We divided the TCE scores in three categories: Absent group (N=16), Present group (N=14) and Emerging group (N=19).

In the Table 5 it is shown that in children where the emotional contagion is Absent at the intake, there is a significant improvement in ADOS scores in the next 2 years ($F_{2,39}$=3.27; p<0.01; $\eta^2_q$=0.14), but then this improvement will stop and after four years the ADOS scores will stable (post hoc: p=0.11).

In children where the emotional contagion is Emerging at the intake, there is a significant improvement in ADOS scores in the next 2 years ($F_{2,39}$=3.27; p<0.01; $\eta^2_q$=0.14), but then this improvement will stop and after four years the ADOS scores will remain stable (post hoc: p=0.19).

In children where the emotional contagion is Present at the intake, there is a significant improvement in ADOS scores after 2 years of treatment ($F_{2,39}$=3.27; p<0.01; $\eta^2_q$=0.14), and this improvement will continue over the next two years (post hoc: p<0.01).

To see which are the best predictors of the severity of the autistic level, we conducted the analysis of the linear regression two years after the beginning of the treatment (Table 6).

The findings show that TCE and UOI are the only predictors of ADOS scores: TCE and UOI high scores correspond to a reduction of ADOS scores over time. Instead IQ and FR predict the decrease of the ADOS scores only for the IQ category 40-75.

## Discussion

The results of this study suggested the reliability of the T.U.L.I.P. protocol to estimate the developmental potentialities in children with autism spectrum disorder as well as to facilitate the differential diagnosis. It is extremely important to isolate a group of children with autism spectrum disorder with positive prognosis and this responds to the DSM-5 criteria.

The dimensional criterion introduced with the DSM-5, as already mentioned, prompts to specify the individual symptomatic characteristics of each child and refers to the current concept of "autisms", instead of autistic disorder. The protocol we used in this research originates from the results already made by administering each of the tests to ASD children, in order to verify the correlation with the

| UOI | ADOS Evolution (Mean and SD) | | | |
|---|---|---|---|---|
| | Assessment 1 | Assessment 2 | Assessment 3 | *p* |
| UOI absent | 19.5 (1.5) | 16.9 (1.8) | 15.7 (2.3) | 0.001 |
| *Confidence interval 95%* | 18.6-20.3 | 15.8-17.9 | 14.4-16.9 | |
| UOI emerging | 15.2 (3.1) | 12.7 (2.9) | 11.5 (3.7) | 0.01 |
| *Confidence interval 95%* | 12.9-17.4 | 10.6-14.7 | 8.8-14.2 | |
| UOI present | 13.8 (4.2) | 9.0 (5.1) | 5.9 (4.6) | 0.001 |
| *Confidence interval 95%* | 11.4-16.2 | 6.3-11.6 | 3.5-8.3 | |

**Table 4:** Mean (SD) of ADOS scores, at first, second and third assessment, in the Absent UOI group, Emerging UOI group and present UOI group.

| TCE | ADOS Evolution (Mean and SD) | | | |
|---|---|---|---|---|
| | Assessment 1 | Assessment 2 | Assessment 3 | *p* |
| TCE absent | 18.33 (3.6) | 15.3 (3.5) | 13.3 (4.2) | 0.001 |
| *Confidence interval 95%* | 16.3-20.3 | 13.3-17.2 | 10.9-15.6 | |
| TCE emerging | 16.7 (3.0) | 14.1 (3.3) | 12.9 (3.6) | 0.001 |
| *Confidence interval 95%* | 14.9-18.3 | 12.2-15.9 | 10.8-14.9 | |
| TCE present | 12.8 (4.4) | 7.8 (5.1) | 4.8 (5.2) | 0.001 |
| *Confidence interval 95%* | 10.1-15.6 | 4.5-11.1 | 1.5-8.2 | |

**Table 5:** Mean (SD) of ADOS scores, at first, second and third assessment, in the Absent TCE group, Emerging TCE group and present TCE group.

| Predictors | β Coefficient | SE | Exp(B) | t | *p* |
|---|---|---|---|---|---|
| IQ scores | -0.052 | 0.065 | -0.202 | -0.810 | 0.42 |
| FR scores | 0.028 | 0.065 | 0.095 | 0.428 | 0.67 |
| TCE scores | -1.300 | 0.529 | -0.263 | -2.455 | 0.01 |
| UOI scores | -1.704 | 0.446 | -0.536 | -3.820 | 0.01 |
| *Costant* | 18.844 | 2.378 | | 7.925 | 0.01 |

**Table 6:** Linear Regression Model: IQ scores, FR scores, TCE and UOI scores as predictors of reduction of ADOS scores.

ADOS as a gold standard to assess the symptom severity. In particular, the Leiter-R had already been administered to 90 ASD children [7], the TCE to 46 ASD children [10] and the UOI to100 ASD children [9].

With this study we wanted to verify the predictability of the three areas (intellectual quotient, emotional contagion and understanding of intention) on the ADOS scores and we want to verify the correlation among all the areas, in ASD children.

As for the first goal, namely to verify if the FR is predictive of future cognitive evolutions, we confirmed what already underlined in previous studies [7,8]. In fact, in the group of children with a low IQ at the intake, seem to be a gradual cognitive improvement in four years of therapy up to reach the IQ score indicated by the FR. For children who have an IQ score at least 15 points higher than the FR there is an improvement in ADOS score.

The predictive value of the Fluid Reasoning suggests the clinical importance of finding a potential closely linked to the flexibility of the mental strategies, such as the abstraction and deduction abilities with discriminating prognostic value in a disease characterized by strong behavioral rigidity of thought.

In fact, the ability of Fluid Reasoning higher than a standard deviation (15 points) compared to IQ, in conditions of intellectual disability, outlines developmental perspectives of progressive increase of cognitive abilities that can be used and socially invested in the quality and quantity of mutual communication, indicated by the improvement in ADOS scores.

As evidence of these considerations it must be stressed that the not assessable IQ (11 of 15 of the not assessable children at the intake remain so even after 4 years of therapy) is a negative index compared to ADOS. Even in those 4 cases where there is an IQ improvement we are

not seeing an ADOS improvement. In such cases we observe a greater adaptability of the child that, however, does not modify the severity of the autistic symptomatology.

With regard to the second goal, that was to verify the predictive value of the UOI on the improvement of autistic symptomatology, the results suggested that children who at the intake had shown a Present ability of UOI, tended to improve over time the ADOS score.

As for the third goal, that is to check the predictive value of an improvement in autistic symptoms through the TCE, the results confirmed that children who at the intake had shown the presence of emotional contagion, both emergent and present, improved over time by changing their ADOS score and maintain constant the level reached.

Despite the ADOS constitutes a gold standard for the assessment of the Autistic Disorder, the level of severity does not allow adequate prognosis.

In fact, although children with better ADOS score have less problematic behaviors it is not for sure that they will have more positive prognosis, as it seems to emerge from our findings.

What is clear from the data is that for the children in this group, who have all less than 7 years, when discovering cognitive and social skills these ones have prevalence in predicting improvement in ADOS scores.

The combination of both indexes (UOI and TCE) in case of a positive response from the child, thus significantly predicts the gradual evolution of symptoms and the positive change in ADOS classification until arriving in some cases to the "No Autism" category showing how much emotional and social skills, more than the cognitive ones, assessed at the intake, can afford to discriminate children that will improve over time.

The research allowed the identification of a subgroup of children who, even before undertaking a course of treatment, shows a greater potential for improvement (in particular through a therapeutic relational oriented approach, which is what we proposed for four years to the 49 children of the sample examined).

A further interesting aspect to underline in these findings concerns the fact that at the first assessment, the average ADOS score is very high

so indicating a severe autistic condition, in all 3 groups. Therefore it is not the ADOS score that indicates the possibility of improvement over time, but it is the presence of emotional and relational potentialities that allows discriminating between children who will improve from those that will improve less.

The T.U.L.I.P. Protocol enables us to identify and isolate children with autistic symptomatology related to an emotional and relational dimension, where the social affection area represents the therapeutic target at which point the treatment.

The usefulness of defining, during the first assessment, a reliable development profile for a positive evolution of the disorder, allows planning a specific intervention, tailored to the child's potentialities, which could, over time, ensure a more harmonious and integrated development of socio-cognitive skills. This work suggests that the T.U.L.I.P. can be a valid and repeatable protocol and, as argued by the most part of the studies about these issues, that there is not a "single autism" and therefore the new frontier is the identification of autism profiles, as individualized as possible. In fact, great attention is currently directed to the definition of the pathogenetic and phenotypic variability of autism [21], to the depth analysis of different fields and levels of functioning, such as the theory of mind and executive functions [22], but also to the quality of life and potential various therapeutic interventions according to the principle of individualization of care based on the definition of development profiles.

The considerations reported so far should take account of a limitation of the present study, represented by the size of the sample (49 children); the sample was composed only by preschool children who were assessed with all three measures (Leiter R, TCE and UOI) in the same evaluation. However, the small sample was monitored over four years of therapy; this gives the research a clinical value as a longitudinal study.

Further studies will be needed, of course, to confirm our findings. In particular, it will be interesting to see if different treatment approaches allow to achieve the same results on the basis of the potential identified through the T.U.L.I.P. Protocol and if, conversely, this Protocol could guide the therapeutic choice.

Another limitation is represented by the few references, but there are still not many studies that have attempted to build one assessment tool to investigate a combination of predictors of improvement in ASD children.

We think that this proposal may represent a first exploration of a new and complex area, namely the identification of prognostic factors and clinical differentiation between different types of autism in that unique therapeutic window represented by developmental age.

## References

1. American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders (DSM–5). Washington, DC.

2. Tordjman S, Somogyi E, Coulon N, Kermarrec S, Cohen D, et al. (2014) Gene environment interactions in autism spectrum disorders: Role of epigenetic mechanisms. Front Psychiatry 5: 1-17.

3. Conradt E, Hawes K, Guerin D, Armstrong DA, Marsit CJ, et al. (2016) The contributions of maternal sensitivity and maternal depressive symptoms to epigenetic processes and neuroendocrine functioning. Child development 87: 73-85.

4. Essex MJ, Shirtcliff EA, Burk LR, Ruttle PL, Klein MH, et al. (2011) Influence of early life stress on later hypothalamic-pituitary-adrenal axis functioning and its covariation with mental health symptoms: A study of the allostatic process from childhood into adolescence. Developmental Psychopathology 23: 1039-1058.

5. Loke YJ, Hannan AJ, Craig JM (2015) The role of epigenetic change in autism spectrum disorders. Front Neurol 6: 107.

6. Hervas A (2016) One autism, several autisms. Phenotypical variability in autism spectrum disorders. Rev Neurol 62 Suppl 1: S9-14.

7. Di Renzo M, Bianchi di Castelbianco F, Petrillo M, Racinaro L, Rea M (2015) Assessment of a long-term developmental relationship-based approach in children with autism spectrum disorder. Psychological Reports: Disability and Trauma 117: 26-49.

8. Di Renzo M, Petrillo M, Bianchi di Castelbianco F (2011) The intellectual potential of the autistic child: new perspectives through the interpretation of the Leiter-R scale, Rome.

9. Di Renzo M, Bianchi di Castelbianco F, Plescia F, Racinaro L, Petrillo M, et al. (2016) The understanding of others' intentions can predict the improvement of symptomatology in children with *Current Pediatric Research, in press*.

10. Di Renzo M, Bianchi di Castelbianco F, Petrillo M, Donaera F, Racinaro L, et al. (2016) The emotional contagion in children with autism spectrum disorders. Austin Journal of Autism and Related Disabilities 2: 1-7.

11. Smith A (2009) The empathy imbalance hypothesis of autism: A theoretical approach to cognitive and emotional empathy in autistic development. The psychological record 59: 489- 510.

12. Di Renzo M, Bianchi di Castelbianco F, Vanadia E, Petrillo M, Racinaro L, et al. (2016) From the emotional integration to the cognitive construction: The developmental approach of turtle project in children with autism spectrum disorder. Autism-Open Access 6: 160-169.

13. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, (DSM-IV). Washington, DC.

14. Lord C, Rutter M, Di Lavore PC, Risi S (2005) ADOS–Autism Diagnostic Observation Schedule. Firenze: OS Organizzazioni Speciali.

15. Lord C, Rutter M, Di Lavore PC, Risi S, Gotham K, et al. (2012) Autism diagnostic observation schedule. Western Psychological Services, Torrance.

16. Roid GH, Miller LJ (2002) Leiter-R-Leiter International Performance Scale-Revised. Firenze:OS Organizzazioni Speciali.

17. Di Renzo M, Stinà M (2011) TEC-Test Emotional Contagion. Firenze: Hogrefe.

18. Hoffman ML (1987) The contribution of empathy to justice and moral judgment. Empathy and its development. Cambridge University Press, New York.

19. Meltzoff AN (1995) Understanding the intentions of others: Re-enactment of intended acts by 18 month old children. Dev Psychol 31: 838-850.

20. Di Renzo M (2007) The meanings of autism: Integration of intellectual and emotional reality in research and in the clinic. Rome.

21. Hervas A (2016) One autism, several autisms. Phenotypical variability in autism spectrum disorders. Rev Neurol 62 Suppl 1: S9-14.

22. Cantio C, Jepsen JR, Madsen GF (2016) Exploring 'The autisms' at a cognitive level. Autism Res.