Diagnostic stability and early developmental trajectory of pervasive developmental disorder using the Autism Diagnostic Interview-Revised

Evoluzione comportamentale nel corso del primo sviluppo del disturbo pervasivo dello sviluppo utilizzando l'Intervista Diagnostica dell'Autismo-Revisionata

Summary

Objective
A sample of 36 children with pervasive developmental disorder (PPD) was evaluated using the Autism Diagnostic Interview-Revised (ADI-R) to assess the natural course of autistic-type symptoms over time.

Methods
The average age at the time of diagnosis (t1) of this sample was 4 years and 4 months (range 2-8). A follow-up occurred after 23.1 months (range from 6 to 84 months) (t2).

Results
All children improved significantly at follow-up, especially in interest, seeking to share own enjoyment with others, use of other's body to communicate, quality of social overtures, reciprocal conversation, and social chat. Total Communication, verbal rituals, and repetitive use of objects also improved significantly (Figs. 1, 2).

Discussion
In the three diagnostic categories, we found a clinical improvement at t2, especially in the communication area; however, pathological language persisted, but social interaction impairments were less prominent. Repetitive behaviours showed more stability with time; moreover diagnosis did not change during this approximately 2-year interval.

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Key words

ADI-R • Pervasive development disorders • Follow-up

The aim of the present study is to monitor the developmental trajectory of autism spectrum symptomatology with a specific scale for autism (Autism Diagnostic Interview-Revised [ADI-R]) in relation to the rarity of the observations in the literature.

Monitoring changes of symptoms overtime is particularly useful for their prognostic and therapeutic implication of individual forms of pervasive developmental disorders (PDD). Nevertheless, there are few follow-ups for the period from 3 to 6 years about the natural history of these disorders with structured instruments [1-9].

According with the *International Classification of Diseases,* 10th edn. (ICD-10) Criteria, PDD are chronic conditions of development that determine before the third year of age severe and generalized impairment in social interaction, communication, and a markedly restricted repertoire of activity and interests. The same diagnostic manual differentiates among the following types of PDD: autism, atypical autism, childhood disintegrative disorders, Asperger's disorder, PDD-not otherwise specified (nos)

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and mental retardation with stereotyped movement and hyperactivity. In the last few years, the number of patients with PDD has increased [10 11]. There are many standardized and semi-structured instruments for the diagnosis and the study of developmental trajectories for these disorders in the first years of life. The most frequently used are: 1) ADI-R (*Autistic Diagnostic Interview*); 2) ADOS (*Autism Diagnostic Observation Schedule*), and 3) CARS (*Childhood Autism Rating Scale*).

The ADI-R[12 13] is standardized instrument that provides an algorithm for the ICD-10 [14]. This instrument is useful for its diagnostic and therapeutic implications. The ADI-R has been used in five studies to assess diagnostic stability across a two-year follow-up in children diagnosed as Autistic and PDD [2 4 7-9]. In the study of Cox et al. [2], diagnostic stability between 20 and 42 months has been confirmed. The studies by Starr et al. [4] and Charman et al. [7], highlighted a clinical improvement between the ages of 2 and 5 years, above all in the communication domain, while progress in social interaction occurs later. Werner's study [8] shows that 27% of the sample, which had the highest degree of social impairment at baseline, reported a significant loss of social ability between the third and the fourth years of age. The ADI-R was used also in Moss's study [9] which has been carried-out on 35 children with a clinical diagnosis of ASD at T1. On initial assessment (mean age 3.5 years) all met ADI-R algorithm criteria for autism. ADI-R assessments were repeated at follow-up (mean age 10.5 years). Changes in ADI-R total, domain and ADI-R algorithm item scores were assessed. Twenty-eight children continued to score above the ADI-R cut-off for autism at follow-up, although significant decreases in ADI-R domain and item scores were also found. Hence, Moss's study shows that while classification of children according to ADI-R criteria generally remained stable between pre-school and elementary school age, many children demonstrated significant improvements in symptom severity. In this study we evaluated a sample of 36 PDD children using the ADI-R to assess the natural course of autistic-type symptoms over time.

Methods and procedures

Participants

To conduct this study, families of 60 children with PDD diagnosis through the ICD-10, who had been discharged by the Division of Children Neuropsychiatry of the University Hospital of Bari between 1997 and 2006 were reached on the phone and asked to participate in a follow-up visit to meet the objectives of this study. Of the 60 families taken into consideration, 36 accepted the proposed follow-up visit, thus constituting the population of the study. The missing families failed to cooperate for a variety of reasons: 1) it was not possible to contact them; 2) they were unable to reach the Division of Children Neuropsychiatry because it was too far away from their residence; 3) due to family or work problems; 4) they did not want their child to undergo an additional clinical control because they had assumed a passive attitude of resignation after the initial diagnosis, preferring to postpone the proposed follow-up visit due to some improvements they felt had occurred in their children, improvement which had increased their expectations for a brighter future.

Therefore, this study was conducted on a sample of 36 children with an average age of 4 years and 4 months (age range 2-8) at diagnosis. We called t1 the first diagnostic and t2 the follow-up visit. The t2 was performed after an average of 2 years (23.1 months: minimum 6 months maximum 84 months).

Evaluation

During the hospitalization at the t1 visit, all patients underwent a comprehensive examination that included clinical observation, *laboratory exams*, *audiometric tests*, electroencephalogram (EEG) and magnetic resonance imaging (MRI) scans meant to exclude the presence of any organic disorders; then, on the basis of factors including age, level of development in speech and language skills, and, in particular, and level of cooperation and compliance from the children, the following standard scales for cognitive assessment were administered: Uzgiritz-Hunt, LEITER-R, WPPSI (*Wechsler Preschool and Primary Scale of Intelligence*), and WISC-R (Wechsler Intelligence Scale for Children Revised). Free observation, playing sessions, and standardized assessment tools specific for autism (ADI-R) were also used to detect any abnormal behaviours.

This study, therefore, was conducted taking into account the ADI-R data reported at t1 in the diagnostic algorithm and t2. The ADI-R is a standardized, semi-structured, investigative interview

for caregivers of individuals with autism, which provides a diagnostic algorithm for the ICD-10 and DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) definition of autism. *The difficulty to use the ADI-R before the age of four is that this instrument has many questions peculiar to the 4-5 year age range, hence, attention must be to the paid to the code between 1-3 years.* An ADI-R diagnosis of childhood autism requires reaching or exceeding cut-off scores in all three ICD-10 symptom domains; there is, impairment in reciprocal social interaction (B = cut-off: 10), communication (C = cut-off: 7-8), repetitive behaviour and stereotyped patterns (D = cut-off: 3), given that abnormality of development is evident before 36 months (A = cut-off: 1). Different cut-off were applied in the communication domain according to whether participants were verbal (8 points) or non-verbal (7 points). The two groups of items called C2V and C3V were administered only to "verbal" subjects, i.e. those subjects able to use at least 3-word sentences in a functional way including both spontaneous language and/or echolalic language or stereotyped language and is comprehensive to other people.

On the basis of the number of the areas examined (A, B, C, D) where the cut-off value exceeded the severity of the scores obtained in the ADI-R diagnostic algorithm, the following three different diagnostic subcategories were found: "infantile autism", "atypical autism", "PDD-NOS".

The data obtained at the time of diagnosis were compared with those obtained by the ADI-R diagnostic algorithm related to the follow-up visit.

Statistical analysis

The data reported in the ADI-R diagnostic algorithm, both at the time of diagnosis and the follow-up visit in question, as well as the data collected from the non-standardized interview were statistically analysed as follows:

- non-parametric tests (Kruskal-Wallis and Mann-Withney) were used to assess differences in the various diagnostic groups;
- the rank-order test with Wilcoxon sign was used to assess levels of improvement of the individual groups of patients;
- contingence tables and coefficient of correlations were used to assess any associations among category variables.

Due to the non-parametric nature of our analysis, the $p < 0.05$ was considered a statistically significant value.

Results

The sample of 36 children was made of 32 boys (88%) and 4 girls (12%) with a boy to girl ratio of 7:1. Clinical data are summarized in Table I.

TABLE I.
Participants' characteristics at t1. *Caratteristiche dei partecipanti al t1.*

	N.	%
Total sample	36	
Infantile autism	22	61
Atypical autism	9	25
PDD nos	5	13
Boy/girl	32/4	88/12
Cognitive functioning:		
• mental retardation	19	52
• no mental retardation	17	48
Language:		
• verbal	14	39
• nonverbal	22	61

The following diagnoses were made according to the score reported in the ADI-R diagnostic algorithm with ICD 10:

- "infantile autism" in 22 children (61%);
- "atypical autism" in 9 children (25%); the atypical nature of autism was linked to the age of onset (after 36 months) in 7 children and to the symptoms themselves in 2 children;
- "PDD-NOS" in 5 children (13 %).

The occurrence of mental retardation detected in most cases by non-structured observation of the behaviour of the child and by the problem-solving strategies he/she adopted, was observed in 19 children of the sample (52%). An appropriate cognitive functioning was observed in the remaining 17 children of the sample.

ADI-R results

On the basis of the capacity of formulating sentences made of three words at least, ADI-R was able to detect in the sample studied 14 (39%) "verbal" children (because they acquire this capacity) and 22 (61%) "nonverbal".

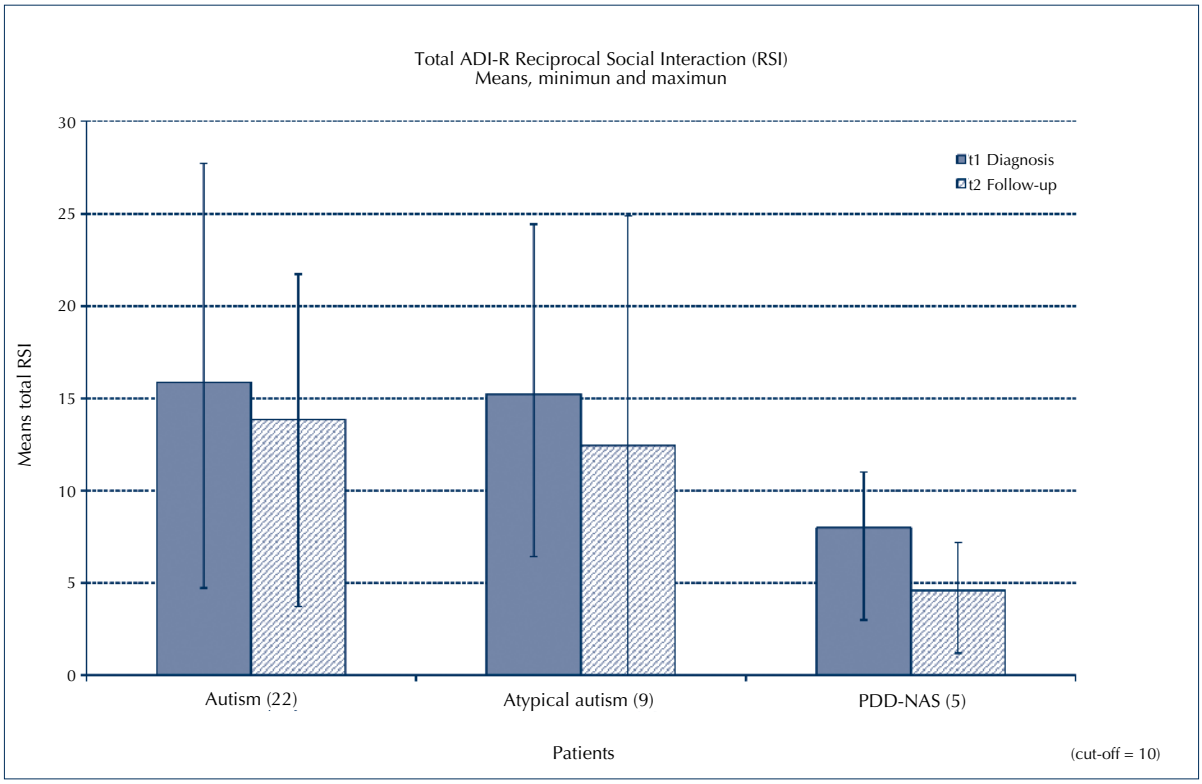

FIGURE 1.
RSI cut-off is 10. *Il cut-off di RSI è 10.*

In comparing the data of the time of diagnosis with those of the follow up the mean value, we have observed improvement of total reciprocal social interaction, whereas total repetitive behaviours and stereotyped patterns are more rigid (Figs. 1, 2).
Total C (Communication) highlights statistical significant improvement: from nonverbal subject become verbal, but often is pathological: with relative failure to initiate or sustain conversational interchange, stereotyped utterances, inappropriate questions, pronominal reversal and neologism/idiosyncratic language.
On 40 items of the ADI-R mean has statistical significant improvement between t1 and t2 only in some items of the entire sample, others are unchanged. We report only the statistically improved mean items between t1 e t2; $p < 0.05$ mean T1-T2 of entire sample were found in:
B2b: Interest in children
B3c: Seeking to share own enjoyment with others
B4b: Use of other's body to communicate
B4c: Quality of social overtures
C2va: Reciprocal conversation
C2vb: Social chat
About repetitive behaviours and stereotyped patterns
D2a: Verbal rituals
D4a: Repetitive use of objects

Statistically significant improvements with $p < 0.05$ were also found in some items of the three different diagnostic subcategories:

Autism

B4b: Use of other's body to communicate
B4c: Quality of social overtures
D4a: Repetitive use of objects

Atypical autism

D4a Repetitive use of objects
PDD nos
B2B Interest in children
C1B Conventional instrumental gestures
Regarding rehabilitative therapies, 50% of patients underwent various therapies between T1 and T2,

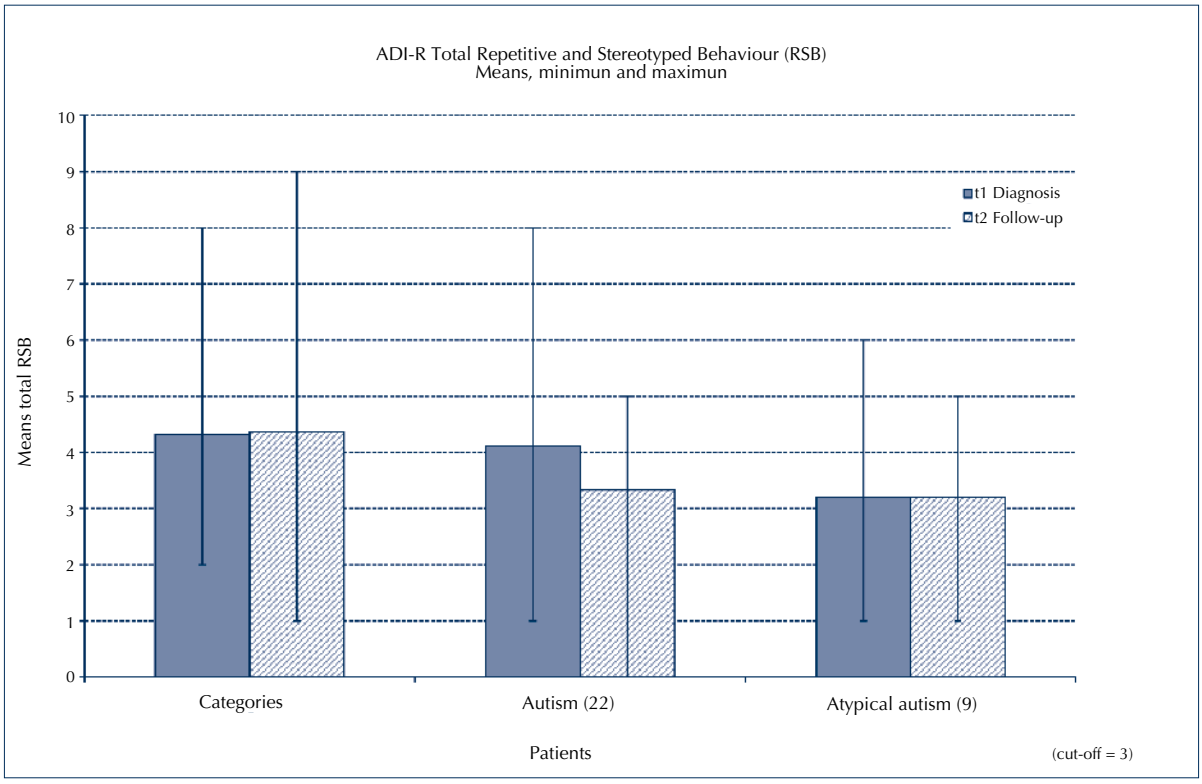

FIGURE 2.
RSB cut-off is 3. *Il cut-off di RSB è 3.*

like psychomotor therapy, psychomotor therapy associated with speech therapy, family therapy, horse therapy, hydrotherapy, music therapy, homeopathy, facilitated communication, holding, Portage and Delacato method, but the available data about their efficacy for the course and outcome of symptoms are not statistically significant in relation to the group that did not perform any kind of therapy in this small sample.

Discussion

The data of literature, relevant to the evolution of the autistic symptomatology highlight a decrement of the autistic symptoms in the most of individuals, even if the disorder is chronic.
In some studies conducted between the ages of 2 and 5 years, using different scales (CARS, Vineland Adaptive Behavioural Scale, Early Developmental Interview, ADOS) some improvements with time have been reported, especially in the area of social interaction compared with the repetitive behaviours which were unchanged independently from the age, while children who had serious social deficits underwent clinical worsening [3 5 6]. Eaves & Ho [6] have considered the stability of diagnosis . In their study, conducted in 43 patients with PDD diagnosis, 10 children (23%) had a change in their clinical picture; 5 children (12%) moved from the PDD group to the autism group; 2 children (5%) moved from the autism group to the PDD-NAS group; 1 child with autism (2%) and 2 children with PDD-NAS developed in time other types of psychopathology.
A few studies used the ADI-R [2 4 7 8] and some of them highlighted a clinical improvement between the ages of 2 and 5 years, mostly occurring in the communication domain, while progress in social interaction occurred later [4 7]. The Werner et al. study [8] showed that 27% of the sample, which had at the baseline the most social deficit, reported a significant loss of ability between 3-4 years of age. Among the studies which used the ADI-R, some also considered the stability of diagnosis. According to Cox et al. [2], there was a stability of diagnosis between 20 and 42 months. Charman et al. [7]

on the other hand, in their study about a sample of 26 children between 2 and 7 years of age who have been suffering from autism since they were 2, found that 22 children (85%) met criteria for autism at 7 years of age; 3 children (12%) at 3 years were already in the atypical autism outline, and just 1 child (3%) did not meet diagnostic criteria for PDD at 7 years of age. A propos of this child, his parents had already a son with autism and worried the second would also be autistic. So when this son was 2 they altered ADI-R answers. It is important to underline that all four children who changed their diagnosis had a high IQ.

The study of Moss et al. [9] examined the stability of scores on the ADI-R from pre-school to elementary school age in children with autism spectrum disorders. Participants were 35 children who, at T1, all had a clinical diagnosis of ASD. On initial assessment (mean age 3.5 years) all met ADI-R algorithm criteria for autism. ADI-R assessments were repeated at follow-up (mean age 10.5 years). Changes in ADI-R total, domain and ADI-R algorithm item scores were assessed. Twenty-eight children continued to score above the ADI-R cut-off for autism at follow up, although significant decreases in ADI-R domain and items scores were also found. Hence, Moss's study shows that despite the stability of classification of children according to the ADI-R criteria between pre-school and elementary school age, many children showed significant improvements in symptom severity.

According to the data of literature, in our sample, in the three diagnostic classes, we find a clinical improvement at t2, especially in the communication area and also in some social interaction areas, although less prominently; the area of repetitive behaviours is more stable with time; moreover, the diagnosis does not change in the interval of time taken into consideration. Limitations of the study were that the time interval between the diagnostic interview and the telephonic follow-up was not a fixed period (range from 6 to 84 months); this may lead to erroneous conclusions about developmental trajectories.

As regards the secondary aims of our study, according to the literature, children with mental retardation had a most important social deficit at t1 and a stability of diagnosis at t2 with less opportunity to achieve a personal and social autonomy [2]. In our sample, it seems that the damage of verbal and extraverbal communication are one only block.

The outcomes examined in the "verbal" and "non-verbal" groups reflect the data of literature on the relationship between best shared attention, best imitation abilities and language abilities [15 16]. So, intellectual functioning, language abilities, shared attention and imitation abilities seem to have an important role for the prognosis.

As for rehabilitative therapies, the available data of their efficacy for the course of symptoms are not statistically significant both due to small sample size and to the variability of different treatments. However, the results of our study suggests that stimulating shared attention (with proper comments), residual imitative abilities (with play activities), pointing something to comment can improve communication abilities especially in not-verbal children at outset of the disease. For the diagnosis impact on the parents professional counselling could be helpful above all in the early phase.

The ADI-R seems to be a careful and useful means for diagnosis, actually in the period examined there are no changes in our sample about the diagnostic outline. *Improvement or stability of diagnosis with ADI-R is confirmed also by clinical data obtained by direct observation of children.*

Furthermore, the ADI-R can be used to follow-up the natural history of children with PDD. Actually, this interview provides from the outset some information about the probable course and outcome of clinical picture of each case and enhances our understanding of the areas that have to be stimulated in particular periods of life. Moreover, on account of different predictive factors, the ADI-R allows us to understand which children and which families need the most important psycho-logical and rehabilitative support for improving the developmental trajectory of PDD.

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