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A comparative study of cognitive and socio-emotional development in children with Rubinstein-Taybi syndrome and children with Autism Spectrum Disorder associated with a severe intellectual disability, and in young typically developing children with matched developmental ages

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ABSTRACT

Background: Cognitive and socio-emotional profiles of children with *CREBBP*-related Rubinstein-Taybi syndrome (RSTS 1), children with Autism Spectrum Disorder (ASD) with severe intellectual disability and developmental ages (DA) under 24 months, and typically developing (TD) children with similar DA were compared.
Participants: Thirty-one children with RSTS 1 (mean chronological age, CA = 59,8 months; 33–87) and thirty children with ASD, matched on CA and DA and developmental quotients (DQ), were compared to thirty TD children (CA ranged from 12 to 24 months).
Methods: Cognitive and socio-emotional developmental levels, DA and DQ were assessed with appropriated tests.
Results: More socio-emotional developmental similarities were observed between TD and RSTS 1 than between TD and ASD children. Clinical groups displayed similar developmental delays in

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cognitive (self-image, symbolic play, means-ends, and object permanence) and socio-emotional domains (language and imitation). Children with RSTS 1 exhibited higher developmental levels in behavior regulation, joint attention, affective relations, emotional expression domains, and a lower developmental level in spatial relations domain.

Conclusions: Common interventions centered on symbolic play, self-image, language, and imitation for both clinical groups, and differentiated interventions centered on spatial abilities for RSTS 1 children and on social abilities for ASD could be used by caregivers were suggested.

What this paper adds?

CREBBP-related Rubinstein-Taybi syndrome (RSTS 1) is the subject of few psychological studies implying proposals for intervention programs, contrastly to ASD. This comparative study of both these clinical groups involved very young typically developing children as a control group. The results showed that children with NDD, compared to TD children, displayed (1) similar developmental abnormalities in cognitive (self-image and symbolic play) and socio-emotional developmental domains (social interaction, expressive language, receptive language, and vocal imitation); (2) among children with RSTS 1, distinct strengths in all socio-emotional domains (behavior regulation, joint attention…) and weaknesses in spatial relations, operational causality, and object permanence domains; (3) in children with ASD, distinct strengths in spatial relations, operational causality, and object permanence, and weaknesses in behavior regulation, joint attention, gestural imitation, affective relations, and emotional expression. The two NDD groups differed in spatial relations (lower level in RSTS 1 than in ASD children), and in the behavior regulation, joint attention, and affective relations domains (higher level in RSTS 1 than in ASD children). Thus, based on these results, recommended interventions can be used interchangeably by professionals and parents of these children. Thus, specific, and now well-known recommended interventions from the field of autism, notably those centered on language, imitation and spatial skills can be proposed for children with RSTS 1 syndrome. Conversely, it would be interesting to analyze and identify specific social and communicative behaviors and strategies used by children with RSTS 1 and try to teach them to children with ASD with low similar developmental ages.

1. Introduction

Since its first description by Rubinstein and Taybi (1963), researchers have investigated the psychological development and behavioral disorders of individuals with Rubinstein and Taybi syndrome (RSTS). Intellectual disability in RSTS is usually associated with an intelligence quotient (IQ) ranging from 25 to 79 (Hennekam et al., 1992; Lacombe et al., 1992; Levitas & Reid, 1998; Stevens et al., 1990), when an average IQ is 100 with average scores ranging from 85 and 115. Additionally, studies of behavioral symptomatology with or without contrast groups have shown abnormalities of children with RSTS, such as difficulty managing emotions, short attention span, motor stereotypies, more excitability and self-stimulation (Galéra et al., 2009), more difficulties in motor action planning and in oculomotor task performance (Cazalets et al., 2017), and a phenotypic profile of repetitive behaviors (Waite et al., 2015). However, they were also described as more jovial and socially interactive (Goots & Liemohn, 1977; Moss et al., 2016) and in comparison with either Down syndrome, Fragile X syndrome, or Autism Spectrum Disorder (ASD), had better abilities on verbal memory development (Waite et al., 2016). Moreover, while they used more repetitive language (including repetitive questions), they had a "functional" type of communication with their environment (Carvey & May Bernhardt, 2009).

Only one study has been conducted investigating the cognitive and socio-emotional developmental profiles of individuals with *CREBBP*-related Rubinstein-Taybi syndrome (RSTS 1) and severe ID (Taupiac et al., 2020). The authors found heterogeneity (Crespi, 2013) in global development, a higher socio-emotional heterogeneity than cognitive heterogeneity, and some specific deficits in language, vocal imitation, and symbolic play abilities. These results were surprising because these developmental heterogeneities and deficits are known to be similarly exhibited in children with Autism Spectrum Disorder, ASD (DSM-5, American Psychiatric Association—APA, 2013) and severe intellectual disability (Adrien et al., 2016; Baron-Cohen, 1987; Bernard et al., 2016; Bernard Paulais et al., 2019; Blanc et al., 2000, 2005; Nader-Grosbois & Seynhaeve, 2008; Seynhaeve & Nader-Grosbois, 2008; Sigman & Ungerer, 1984; Thiébaut et al., 2010; Thiemann-Bourque et al., 2019; Wetherby et al., 1998; Wing et al., 1977). Moreover, developmental disparities were found in children with ASD with and without intellectual disabilities (Mecca et al., 2014; Nowell et al., 2015) in the development of non-verbal and verbal intelligence (Ankenman et al., 2014; Joseph et al., 2002; Nowell et al., 2015), of expressive and receptive language abilities (Kwok et al., 2015), and of motor coordination skills (Fournier et al., 2010; Gandotra et al., 2020; Page & Boucher, 1998; Provost et al. 2007). This developmental variability was also recently identified in infants at high-risk for ASD, in the domains of socio-communicative and linguistic and object exploration skills (Bruyneel et al., 2019; Franchini et al., 2018; Kaur et al., 2015; Srinivasan & Bhat, 2019) and is already present in the early development of infants later diagnosed with ASD (Brisson et al., 2012, 2014; Osterling & Dawson, 1994). Based upon these various findings, several early intervention proposals have been recommended for children with ASD (Aldred et al., 2004; Dawson et al., 2010; Kasari et al., 2001; Schreibman et al., 2015).

While Taupiac et al. (2020) noted similar developmental delays between RSTS 1 and ASD children, they also noted the developmental profiles of children with RSTS 1 were characterized by better developmental levels than children with ASD in the domains of joint attention, behavior regulation, social interaction, and affective relations. However, these similarities and differences found between these two syndromes regarding developmental delays were based on results obtained from two different studies, including on the one hand a significant international sample of 110 children with ASD (Bernard Paulais et al., 2019) and on the other hand a small

group of 23 children with RSTS 1 (Taupiac et al., 2020) in which developmental levels, ages, and quotients were not strictly matched and chronological ages were not strictly similar.

1.1. Study objective

While developmental heterogeneity and its specific characteristics are truly relevant to understanding the nature of neurodevelopmental disorders (NDD) (Lombardo et al., 2019), the objective of this study was to examine and compare the global, cognitive, and socio-emotional developmental profiles of children with RSTS 1 and children with ASD with severe ID, who were strictly matched on developmental ages, quotients, and chronological ages. Because Thiébaut et al. (2021) found that there was a slight cognitive and socio-emotional developmental heterogeneity in a group of 65 typically developing children (TD) with developmental ages comprised between 4–24 months, this study also included a group of typically developing children to show evidence of developmental levels and profiles differences and similarities between these three groups. Thus, this study sought (1) to identify whether both clinical groups' profiles were different from those of TD children matched for developmental age, (2) whether there were common characteristics to both NDD groups, and (3) to determine what disabilities and abilities were significantly different between the NDD groups.

Our first hypothesis was that children with neurodevelopmental disorders (NDD) with similar developmental ages would exhibit lower cognitive and socio-emotional developmental levels, and more heterogeneous and different developmental profiles compared to TD children. Secondly, we hypothesized that children with RSTS 1 would exhibit higher mean developmental levels in some socio-emotional abilities but similar deficits in cognitive areas than children with ASD, and different developmental heterogeneities profiles.

2. Materials and methods

2.1. Ethical approval

This study received ethical approval from the "French Bioethics and Clinical Research and Data Legislation Protection" board. Consent for each child's participation was obtained from a parent or guardian. This study was conducted in partnership with the French RSTS 1 Association.

2.2. Participants

2.2.1. Children with CREBBP-related Rubinstein-Taybi syndrome (RSTS 1)

Among a clinical population of about one hundred children with RSTS from the Medical Genetics Department, a subgroup of thirty-one children with RSTS 1 (18 boys and 13 girls) with a mean chronological age of 4 years and 11 months were selected based on developmental age inferior to 30 months and severe intellectual disability (Table 1). There was no significant difference between ages according to gender. Diagnoses of RSTS 1 were carried out by expert geneticists based on clinical examination and were confirmed by the identification of a CREBBP mutation (gene deletion or point mutation), known to be associated with a severe ID (Fergelot et al., 2016; Petrij et al., 1995). Developmental Delay and Intellectual disability were assessed with the Brunet-Lézine Revised scale (Brunet & Lézine, 2001) which assesses psychomotor development in posture, oculo-manual coordination, language, and sociability domains in children whose developmental age is comprised between 1 and 30 months. For each child, a Global Developmental Age (GDA) and a Global Developmental Quotient (GDQ) were calculated. The GDQ was obtained by dividing the GDA by chronological age, multiplied by 100 (Table 1). At our knowledge, no research shows evidence of some differences in psychomotor development according to gender.

2.2.2. Children with ASD

Thirty French children with ASD (25 boys and 5 girls), whose mean chronological age was 4 years and 10 months, were selected from the SCEB international database to be strictly matched one to one to the group of children with RSTS 1 on global developmental ages and quotients, and chronological ages. Developmental Delay was assessed with the Brunet-Lézine Revised scale (Brunet & Lézine, 2001). The selected children with ASD were referred by two Child and Adolescent Psychiatry Departments (N = 14 and N = 6), and by

Table 1
Demographic data of the three groups.

	Chronological age			Developmental age			Developmental Quotient		
	Mean (months)	SD	Range (months)	Mean (months)	SD	Range (months)	Mean	SD	Range
ASD N = 30 25 boys; 5 girls	58; 6	17.92	32–92	17; 20	3.91	10–28	33.19	12.50	16–59
RSTS N = 31 18 boys; 13 girls	59; 8	17.01	33–87	17; 13	3.93	9; 28.25	32.50	10.17	16.25–54.50
TD N = 30 13 boys; 17 girls	17; 23	3.82	12–24	18; 12	4.29	12–24	103.62	9.36	83–128

a Psychology Practice (N = 10). The diagnoses of ASD and ID as a comorbidity were performed by child psychiatrists and psychologists specialized in ASD and other neurodevelopmental disorders, based on DSM 5 criteria and confirmed by a CARS assessment (Schopler et al., 1988). The mean CARS score was 40.43, indicating severe autistic symptomatology. There was no significant sex difference (at the $p < .05$ level) for the CARS scores ($F(1, 28) = 0.88$, $p = 0.36$).

2.2.3. Control group of TD children

Thirty young TD children between 12 and 24 months old (half of which were between 12 and 17 months and 29 days, and the other half between 18 and 24 months old) were selected from the French SCEB database to match each of the children with ASD and with RSTS 1 (Table 1) on developmental ages assessed with the Brunet-Lézine Revised scale (Brunet & Lézine, 2001). These children were recruited from public nurseries and from the professional or social environment of the psychologists participating in the study.

Developmental age values were normally distributed (D Kolmogorov-Smirnov = 0.07, $p = 0.73$).

There was no significant difference (at the $p < .05$ level) between the mean chronological ages of the RSTS 1 and ASD groups ($F(1, 59) = 0.56$, $p = 0.81$), but the difference was significant between the TD and RSTS 1 groups ($F(1, 59) = 170.1$, $p < 0.001$) and between the TD and ASD groups ($F(1, 58) = 146.1$, $p < 0.001$). There was no significant difference between mean chronological ages by sex ($F(1, 85) = 2.49$, $p = 0.118$), and no interaction effect (sex) within the groups ($F(2, 85) = 0.99$, $p = 0.375$).

There were no significant differences between mean global developmental ages for each group ($F(2, 85) = 0.38$, $p = 0.363$), for sex ($F(1, 85) = 0.05$, $p = 0.821$), but a low interaction effect between sex and group variables was observed ($F(2, 85) = 3.61$, $p = 0.031$). These results confirm that both clinical groups of children were matched for developmental ages with typically developing children.

There were no significant differences between mean global developmental quotients of both clinical groups of children (RSTS 1 and ASD) ($T(59) = -0.23$, $p = 0.816$). The clinical groups were not matched on developmental quotients to TD group. In fact, since the TD group was equivalent to the RSTS 1 and ASD groups for the developmental age criterion assessed with the Brunet-Lézine Revised scale (Brunet & Lézine, 2001) but differed from the RSTS 1 and ASD groups for the chronological age criterion ; consequently, the TD group differed from the RSTS 1 and ASD groups for the Development Quotient criterion, since the quotient is a ratio of developmental age to chronological age.

2.3. Measures

2.3.1. Social Cognitive Evaluation Battery (SCEB)

The Socio-emotional Cognitive Evaluation Battery (SCEB; Adrien, 2007) is based on widely accepted models of child development (Fischer, 1980; Piaget, 1977) and was used to carry out the developmental assessment of children in the study. The SCEB assesses the developmental levels (Level 1 = 4–8 months, level 2 = 8–12 months, level 3 = 12–18 months and level 4 = 18–24 months) in seven domains of the cognitive area: self-image, symbolic play, object-relation schemata, operational causality, means-ends relations, spatial relations, and object permanence, and in nine domains of the socio-emotional area: behavior regulation, social interaction, joint attention, expressive language, receptive language, vocal imitation, imitation of gestures, affective relations, and emotional expression. A developmental level score from 1 to 4 was determined for each of the 16 domains which provides a developmental profile for each child. The overall average level score, as well as cognitive and socio-emotional development scores were calculated. Developmental heterogeneities were calculated based upon differences between indices of heterogeneity for global development (16 domains), cognitive development (7 domains), and socio-emotional development (9 domains). These indices corresponded to the mean difference (in absolute values) between all the level scores *(1–4)* of each domain multiplied by 10. They ranged from 0 (no heterogeneity) to 16 (maximum heterogeneity). Moreover, developmental heterogeneity was measured in searching significant differences between mean developmental levels in both cognitive and socio-emotional areas in each of the three groups.

All scores of the SCEB presented appropriate reliability and validity according to the usual psychometric criteria (Adrien, 2007; Thiébaut et al., 2010).

2.4. Procedure

The developmental assessment of each child with RSTS 1 was carried out by the second author in a specific room of the department of medical genetics between 2008 and 2019, in one sitting.

Each participant with ASD was accompanied by his/her parents to the clinical service and was assessed in a single 30-to-45-minute session in a suitable room by psychologists experienced with children presenting with ASD and ID, and familiar with the SCEB material (first, fourth, fifth, sixth and seventh authors).

Assessment of each TD child was carried out in his/her home in a suitable room for this purpose. The mother was present for her child's examination and observed him/her without intervening.

Written and informed consent was obtained from the legal guardians who were informed of the non-invasive nature of the research and the confidentiality of the data. Furthermore, the systematic use of video recordings during evaluations was subject to written consent from the families.

2.5. Data analysis

A mixed between-within subjects' ANOVA was conducted to compare the effect of group on mean scores of global, cognitive, and socioemotional developmental levels. For the pairwise comparisons, probability was adjusted (for the number of tests) according to the

Bonferroni method. By multiplying pairwise comparisons (3 when comparing 3 groups), the probability of obtaining a significant difference by random effect when it is not significant is increased. Bonferroni probability adjustment for analytical comparisons is applied to minimize the risk of concluding that a difference is significant when it is not. The probabilities displayed are those corrected. For the developmental heterogeneity indices, not all distributions were compatible with the Gaussian distribution therefore comparative analyses were carried out using the non-parametric Kruskal-Wallis test and the pairwise comparisons using the Mann-Whitney *U* test with a probability adjustment (for the number of tests) according to the Bonferroni method. The same tests were used for inter-group comparisons of levels of development according to SCEB domains. Analyses were performed with R (R Development Core Team, 2008).

3. Results

3.1. Intergroups comparative analysis of mean global, cognitive, and socioemotional developmental levels

The SCEB global, cognitive, and socio-emotional scores showed no significant difference with normal distribution.

Mean scores of global, cognitive, and socio-emotional development are presented in Table 2 and profiles of these scores are presented in Fig. 1.

There were significant differences in the means of developmental levels across groups ($F(2, 88) = 16.14$, $p < .001$), across the global, cognitive, and socio-emotional mean scores ($F(2, 176) = 18.62$, $p < .001$), and a significant interaction effect of the groups' developmental levels ($F(4, 176) = 24.88$, $p < .001$).

The comparative analysis of mean global developmental levels showed evidence of significantly higher developmental levels in the TD group when compared to RSTS 1 groups ($T(59) = -4.59$, $p < 0.001$) and ASD groups ($T(58) = -5.58$, $p < 0.001$), but there was no significant difference between the RSTS 1 and ASD groups ($T(59) = 0.99$, $p = 0.88$), although the RSTS 1 group mean developmental level was slightly higher than in ASD.

Concerning mean cognitive developmental levels, comparative analysis showed evidence of significantly higher developmental levels in the TD group when compared to RSTS 1 groups ($T(59) = -4.82$, $p < 0.001$) and ASD groups ($T(58) = -3.46$, $p = 0.006$), but there was no significant difference between the RSTS 1 and ASD groups ($T(59) = -1.41$, $p = 0.374$), although the RSTS 1 group mean developmental level was slightly lower than in ASD.

Comparative analysis of mean socio-emotional developmental levels showed evidence of significantly higher developmental level in the TD group when compared to RSTS 1 groups ($T(59) = -4.10$, $p < 0.001$) and ASD groups ($T(58) = -6.38$, $p < 0.001$), and of higher developmental level in the RSTS 1 group when compared to the ASD group ($T(59) = -2.78$, $p = 0.013$).

3.2. Comparative analysis of developmental heterogeneity indices

Median scores indices for the three groups are presented in Table 3.

Regarding the Global Heterogeneity Index (GHI), there were significant differences in the median scores of the GHI by group (χ^2 (2, $N = 91$) $= 36.05$, $p < 0.001$). Pairwise comparisons showed significantly lower GHI in the TD group when compared to the RSTS 1 ($p < 0.001$) and ASD groups ($p < 0.001$), but not between the ASD and RSTS 1 groups ($p = 0.40$), although GHI of children with RSTS 1 was lower than ASD.

Regarding the Cognitive Heterogeneity Indices (CHI), there were significant differences in the median scores of the CHI between groups (χ^2 (2, $N = 91$) $= 30.43$, $p < 0.001$). Pairwise analysis showed a significantly lower CHI in the TD group when compared to the RSTS 1 ($p < 0.001$) and ASD groups ($p < 0.001$), and in the RSTS 1 group when compared to ASD ($p = 0.037$).

Regarding the Socio-emotional Heterogeneity Indices (SHI), there were significant differences in index median between groups (χ^2 (2, $N = 91$) $= 24.44$, $p < 0.001$). Pairwise comparisons showed significantly lower SHI in the TD group when compared to the RSTS 1 ($p < 0.001$) and ASD groups ($p < 0.001$), but there was no significant difference between the RSTS 1 and ASD groups ($p = 1.$), although SHI was slightly higher in RSTS 1.

3.3. Comparative analysis of median developmental levels in the cognitive and socio-emotional domains

Profiles of median cognitive and socio-emotional developmental level scores of each group in each of the sixteen domains are presented in Fig. 2.

Median scores of each SCEB developmental domain for each group are presented in Table 4.

Comparative analysis of median developmental level scores between the groups (between variables) showed evidence of significant

Table 2
Mean developmental levels and standard deviation scores of global, cognitive, and socio-emotional development.

Developmental levels SCEB	Mean			SD		
	ASD	RSTS	Typical	ASD	RSTS	Typical
Global	2.65	2.80	3.41	0.58	0.57	0.47
Cognitive	2.97	2.75	3.43	0.59	0.65	0.44
Socio-emotional	2.40	2.84	3.39	0.68	0.54	0.52

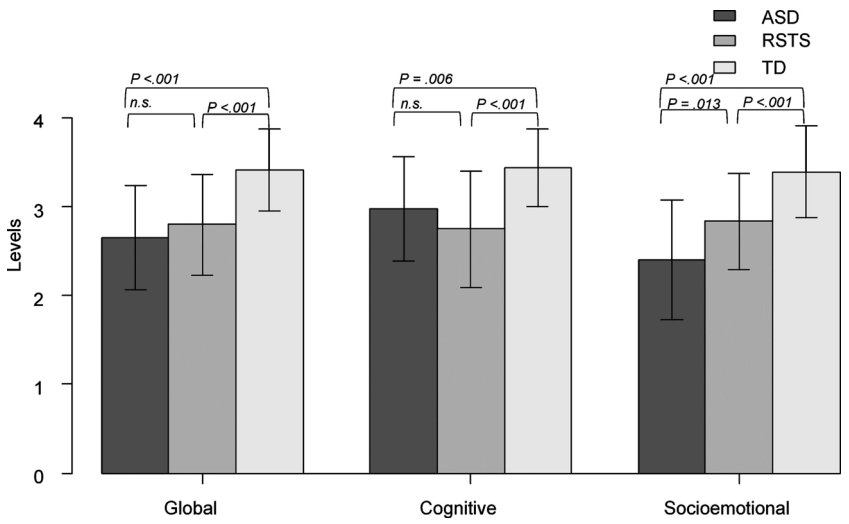

Fig. 1. Profiles of mean global, cognitive, and socio-emotional developmental level scores for the three participant groups: RSTS, ASD, and Typically Developing (TD) children (Developmental levels from 1 to 4).

Table 3
Mean developmental levels and standard deviation scores of global, cognitive, and socio-emotional development.

	Median			Mann-Whitney Test W (Wilcoxon) metric and probability adjusted (Bonferroni)		
Heterogeneity	ASD	RSTS	Typical	ASD/RSTS	ASD/Ty	RSTS/TY
Global	9.23	8.13	4.63	W = 361, p = .40	W = 778.5, p <.001	W = 840.5, p <.001
Cognitive	7.61	6.11	3.87	W = 295.5, p = .037	W = 784.5, p <.001	W = 718.5, p <.001
Socio-emotional	9.14	9.52	5.02	W = 495, p = 1.00	W = 701.5, p <.001	W = 793, p <.001

differences. Results are presented in Table 5.

Children with RSTS 1 had significantly lower mean developmental scores than TD children on six of the cognitive domains: self-image, symbolic play, object schemata relation, operational causality, spatial relation, and object permanence; and in four socio-emotional domains: social interaction, receptive language, expressive language, and vocal imitation. Children with ASD had significantly lower developmental levels than TD children in three cognitive domains: self-image, symbolic play, and object relation schemata; and in all the nine socio-emotional area domains.

Developmental levels of both clinical groups of children were significantly lower than TD children on three cognitive domains: self-image, symbolic play, and object relation schemata; and on four socio-emotional domains: social interaction, expressive language, receptive language, and vocal imitation.

Children with RSTS 1 had a significantly lower developmental level than children with ASD in only one cognitive domain, spatial relations, but their developmental levels were significantly higher in three socio-emotional domains, behavior regulation, joint attention, and affective relations. The ASD group had a significantly lower developmental level from both the TD and RSTS 1 groups in the joint attention domain. Only the means-ends domain did not differentiate the three groups of children.

Children with RSTS 1 had many less socio-emotional domains (N = 4) than cognitive domains (N = 6) that differentiated them from TD children, in contrast to children with ASD (socio-emotional domains = 9 and cognitive domains = 4). Additionally, both groups of children with NDD had developmental delays in common in seven domains which differentiated them from TD children: three cognitive domains (self-image, symbolic play, object relation schemata) and four socio-emotional domains (social interaction, receptive and expressive language, and vocal imitation). However, unlike children with ASD, children with RSTS 1 had three cognitive domains (operational causality, spatial relations, and object permanence) which were significantly delayed compared to the TD group. The ASD group had five socio-emotional domains (behavior regulation, joint attention, gestural imitation, affective relations, and emotional expression) which were significantly delayed compared to TD children.

4. Discussion

This study showed evidence that cognitive and socio-emotional developmental profiles of children with neurodevelopmental disorders such as RSTS 1 and ASD with severe ID (who were strictly matched on chronological and developmental ages and quotients) were different from the developmental profiles of a group of very young TD children strictly matched on developmental ages (12–24 months). The NDD children had lower developmental levels than the TD group, which highlights their different and atypical

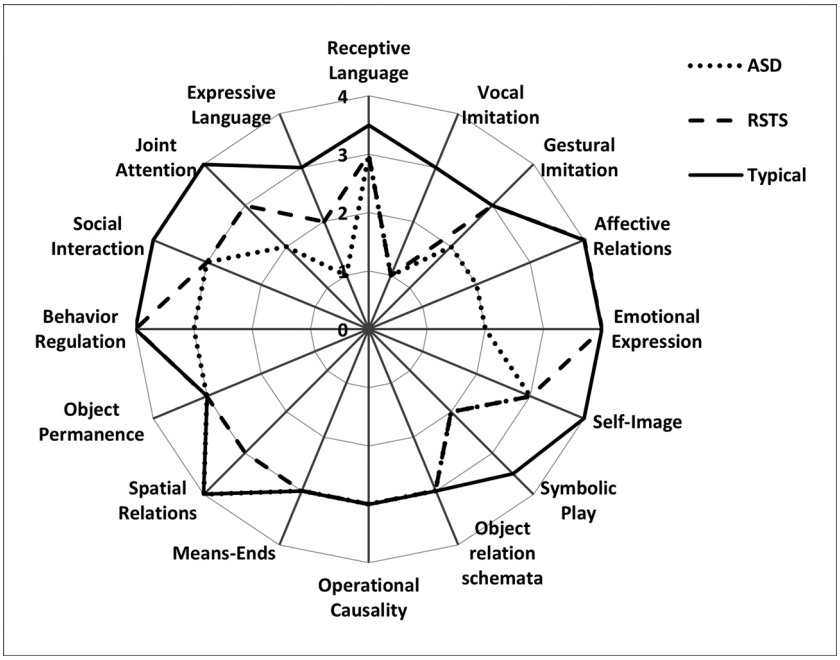

Fig. 2. Median developmental level score profiles from the 16 SCEB cognitive and socio-emotional domains for the three groups of ASD, RSTS, and TD children. Scores can range from 1 to 4.
Legend:
Socio-emotional domains: BR: Behavior Regulation, SI: Social Interaction, JA: Joint Attention, EL: Expressive Language, RL: Receptive Language, VI: Vocal Imitation, GI: Gestural Imitation, AR: Affective Relations, EE: Emotional Expression
Cognitive domains: SI: Self-Image, SP: Symbolic Play, Sch: Object relation schemata, OC: Operational Causality, ME: Means-Ends, SR: Spatial Relations, OP: Object Permanence

Table 4
Median developmental level scores on the SCEB cognitive (1 to 7) and socio-emotional (8 to 16) domains for each group of children.

Domains of the SCEB	ASD Median	RSTS	Typical
1 Self-Image	3	3	4
2 Symbolic Play	2	2	3.5
3 Object relation schemata	3	3	3
4 Operational Causality	3	3	3
5 Means-Ends	3	3	3
6 Spatial Relations	4	3	4
7 Object Permanence	3	3	3
8 Behavior Regulation	3	4	4
9 Social Interaction	3	3	4
10 Joint Attention	2	3	4
11 Expressive Language	1	2	3
12 Receptive Language	3	3	3.5
13 Vocal Imitation	1	1	3
14 Gestural Imitation	2	3	3
15 Affective Relations	2	4	4
16 Emotional Expression	2	4	4

developmental trajectories and profiles. Furthermore, the study showed that cognitive development heterogeneity was significantly lower in children with RSTS 1 than ASD and that the NDD groups displayed similar developmental delays in cognitive (self-image, symbolic play, means-ends, and object permanence) and socio-emotional domains (language and imitation). However, children with RSTS 1 exhibited significantly higher mean developmental levels in the socio-emotional area, and domains such as behavior regulation, joint attention, affective relations, emotional expression, and a significantly lower developmental level in one cognitive domain (spatial relations) than children with ASD.

Table 5
Differences in median developmental levels between the three groups in all the 16 SCEB cognitive (1 to 7) and socio-emotional domains (8 to 16).

SCEB Domains	Chi^2 Kruskall-Wallis (dl = 2)	p.	Mann-Whitney U test - probability		
			Typical/ASD	Typical/RSTS	ASD/RSTS
1 Self-Image	13.25	0.001	0.003	0.011	1.000
2 Symbolic Play	32.90	<0.001	<0.001	<0.001	1.000
3 Object relation schemata	14.46	0.001	0.005	0.002	1.000
4 Operational Causality	9.64	0.008	1.000	0.008	0.074
5 Means-Ends	2.81	0.245	1.000	0.300	0.650
6 Spatial Relations	12.92	0.002	1.000	0.002	0.038
7 Object Permanence	9.54	0.008	0.339	0.008	0.336
8 Behavior Regulation	20.63	<0.001	<0.001	1.000	0.001
9 Social Interaction	22.35	<0.001	<0.001	0.019	0.070
10 Joint Attention	18.74	<0.001	<0.001	0.062	0.015
11 Expressive Language	27.54	<0.001	<0.001	<0.001	1.000
12 Receptive Language	13.57	0.001	0.009	0.002	1.000
13 Vocal Imitation	33.90	<0.001	<0.001	<0.001	0.530
14 Gestural Imitation	9.13	0.010	0.010	0.240	0.460
15 Affective Relations	17.71	<0.001	<0.001	0.296	0.008
16 Emotional Expression	8.47	0.014	0.027	1.000	0.061

This study had a limitation relative to the assessment context of the TD children. TD children were tested in a different context than the clinical groups. They were examined at home, in a familiar room and in presence of their parents, while children with NDD were tested in an unusual room and without their parents. This difference in environment might impact findings by facilitating the responses of typical children, even though the psychologist assessors were expert in the examination of children with neurodevelopmental disorders and exhibited regulated behaviors adapted to each of them.

4.1. Comparative analysis of mean global, cognitive, and socio-emotional levels of development

Results showed that all mean developmental levels were significantly lower in children with RSTS 1 and children with ASD than in TD children. Thus, although TD children were strictly matched on developmental ages with both clinical groups, a wide range assessment with a tool such as the SCEB identified differences in mean levels of the development of various cognitive and socio-emotional skills. Moreover, we observed that children with RSTS 1 had mean global and cognitive developmental levels which were almost equal to those of children with ASD. This result highlights similarities between children with these neurodevelopmental disorders and thus confirms the relevance of a dimensional approach in developmental psychopathology (Rutter, 2005). This would be useful for the identification of similarities and differences in neurodevelopmental disorders with the purpose of providing similar or different treatment interventions as appropriate. Moreover, results showed that the mean socio-emotional developmental level was significantly higher in children with RSTS 1 than in children with ASD, supporting previous findings on the one hand that RSTS 1 children were socially interactive and used functional communication, and on the other hand, that developmental symptomatology in ASD with severe ID is well characterized by delays and deficits in the socio-emotional area and is different from ID without ASD (Nader-Grosbois, 1999; Nader-Grosbois & Seynhaeve, 2008; Sigman & Ungerer, 1984).

4.2. Comparative analysis of developmental heterogeneity indices

Global developmental heterogeneity corresponding to mean difference between developmental levels of the sixteen domains was more significant in children with RSTS 1 and with ASD than in TD children, in whom development profiles were globally homogeneous and corresponded to normative data for global heterogeneity indices (Thiébaut et al., 2021). Firstly, this result confirms that the SCEB is sensitive to developmental disorders in children, and secondly, that the SCEB assessment of TD children's development corresponds well with the theoretical models of typical development (Fischer, 1980; Piaget, 1977) that underlie its elaboration and construct (Thiébaut et al., 2010, 2021).

Global heterogeneity was lower in children with RSTS 1 (GHI = 8,13) than in children with ASD (GHI = 9,23) but was not significantly different. In fact, among the group with ASD, expressive language and vocal imitation abilities were the most delayed (level 1 = 4–8 months) while the spatial relations ability had the highest developmental level (level 4 = 18–24 months), attesting to the verbal/non-verbal abilities discrepancy in ASD (Nowell et al., 2015). Regarding the cognitive heterogeneity index which corresponds to mean difference between the developmental levels of the seven cognitive domains, there was a significant difference between children with RSTS 1 and ASD compared to TD children. This difference was less important between TD children and children with RSTS 1 who had a significantly lower heterogeneity index (CHI = 6,11) than children with ASD (CHI = 7,61). This shows evidence that children with RSTS 1 and a severe ID are characterized by less disparity in cognitive developmental levels than children with ASD, whose heterogeneous profiles may be explained by a higher gap between the developmental level in spatial ability (level = 4) and the other cognitive abilities (level from 2 to 3). Regarding socio-emotional development including the nine domains, both groups of

children with neurodevelopmental disorders exhibited a significantly more heterogeneous developmental profile than TD children but there was no statistically significant difference between indices of the clinical groups. Heterogeneity in the clinical groups may be explained by their similar severe delays in expressive language and vocal imitation domains.

4.3. Comparative analysis of median cognitive and socio-emotional levels of development

Results showed evidence that children with RSTS 1 exhibited fewer skills with deficits than children with ASD, when compared to TD children. Specifically, in children with RSTS 1, only three domains showed deficits (receptive language, expressive language, and vocal imitation) while in ASD children, the deficits concerned all the nine socio-emotional domains (behavior regulation, social interaction, joint attention…). This supports previous findings indicating that developmental dysfunction in ASD is characterized by deficits and delays in socio-communicative skills, and particularly in joint attention (Mundy, 1995; ; Mundy & Crowson, 1997; Wetherby et al., 1998) which is the only skill which differentiated them from both TD children and children with RSTS 1 and that is known to be specifically disturbed in the early neurocognitive development of infants later diagnosed as ASD (Mundy, 2018).

However, compared to TD children, children with RSTS 1 did exhibit some of the deficits and delays which are common in children presenting with ASD in the cognitive area: self-image, symbolic play, object relation schemata, and in the socio-emotional area, receptive language, expressive language, and vocal imitation. Thus, some of the deficits and developmental delays which characterize children with ASD, such as self-recognition (Dawson & McKissick, 1984; Neuman & Hill, 1978), symbolic function evidenced by the misuse of substitutive play (Bernard Paulais et al., 2019; Jarrold et al., 1993; Wing et al., 1977), and expressive and receptive language delays (Kim et al., 2014) might also characterize children with RSTS 1 and a severe ID (Taupiac et al., 2020). This result indicates that children with a severe intellectual disability, with or without autism, might exhibit similar deficits in sensorimotor and communicative development (Nader-Grosbois, 1999; Reisinger et al., 2019; Seynhaeve & Nader-Grosbois, 2008). However, since the expressive and receptive language domains in the SCEB only assess lexical and semantic development, it would be relevant to explore differences and similarities in the other language components (phonological, pragmatic, syntactic). Indeed, children with ASD tend to display prominent problems in pragmatic communication ability (Baron-Cohen, 1988), while children with RSTS 1 may develop this ability although without, or with poor and rare, pre-verbal and verbal productions (Carvey & May Bernhardt, 2009).

Furthermore, since both the clinical groups exhibited motor dysfunction (Cazalets et al., 2017; Gandotra et al., 2020), it would be interesting to explore language development with a new assessment method centered on speech motor function (Sullivan et al., 2013) which might be very relevant for children with RSTS 1. Additionally, compared to TD children, children with RSTS 1, but not children with ASD, showed developmental delay in three cognitive domains: spatial relations, operational causality, and object permanence. These specific delays in non-verbal abilities might be explained by dysfunction in the manipulation of objects, such as the coordination of sensorimotor actions (Cazalets et al., 2017) to solve spatial and causal problems and to search for a hidden object.

Which domains specifically differentiated children with ASD from those presenting with RSTS 1? While mean cognitive developmental level was lower in children with RSTS 1, results indicated that only one of the seven cognitive skills differentiated the two groups: it was the ability to establish spatial relations between objects, by embedding puzzle pieces, stacking cubes, and storage activities. This domain's developmental level was lower in children with RSTS 1, confirming the noticeable delay in this skill involving motor abilities in children with this disorder (Cazalets et al., 2017). Additionally, the mean developmental levels of three socio-emotional domains, behavior regulation, joint attention, and affective relation, were significantly higher in children with RSTS 1 than in children with ASD (Charman, 2003; Kasari et al., 1990; Mundy, 1995). This also confirmed the better social skills that can be observed in children with RSTS 1 (Goots & Liemohn, 1977; Moss et al., 2016).

This study also investigated affective relation skills in the socio-emotional domain. The assessment of this skill on the SCEB is based upon specific models of psycho-affective development (Spitz, 1968; Trevarthen, 1979) and focuses on the development of the self/-other organization (Aitken & Trevarthen, 1997). In this study, children with RSTS 1 presented less significant delays in affective relation skills (level 4 = 18–24 months) than children with ASD (level 2 = 8–12 months). This finding confirms the ability among severely intellectually challenged children with RSTS 1 to establish affective relations towards other people by affirmative and socio-adaptive behaviors, and to demonstrate self-awareness, despite their communicative abilities (expressive and receptive language and vocal imitation) being as severely delayed as those observed in children with ASD (Taupiac et al., 2020). This result corroborates previous findings among children with ASD regarding significant disability (Hobson, 1995; Muratori & Maestro, 2007; Mundy et al., 2010).

5. Conclusion

The finding that children with RSTS 1 and ASD with a severe ID and low developmental levels exhibited several similarities in cognitive and socio-emotional developmental profiles is significant and implies that professionals who work with children with RSTS 1 should be encouraged to use the various programs and Naturalistic Developmental Behavioral Interventions developed for children with ASD, notably those which are centered on developmental delays in language, imitation, and symbolic activities as early as possible (Aldred et al., 2004; Dawson et al., 2010; Green et al., 2010; Schreibman et al., 2015). For example, relative to delay in vocal and verbal imitation, remediation could use strategies like slowing down the speed of verbal and vocal information, which is known to improve verbal cognition and behavior in ASD (Tardif et al., 2017) and so, might increase language development in children with RSTS 1. Moreover, for these children, specific interventions should be centered on spatial abilities implying motor activity. In addition, the finding that children with ASD with low developmental levels exhibited specific abnormalities in social communication skills that are known to emerge in TD children in the two first years of life again highlights the need to develop very early intervention programs

including parents and centered on these neurodevelopmental disabilities (Abalawi & Alkhatib, 2019; Kasari et al., 2001; Mundy & Crowson 1997; Mundy et al., 2010; Rogers, 1996). Future research might comparatively explore the functioning in language, imitation, and symbolic play in both these clinical groups in a detailed way to show evidence of particularities. Moreover, it would be interesting to study the developmental trajectories in these domains of children with RSTS 1 with a severe ID who benefited from early interventions centered on these abilities.

Availability of data and materials

The data used and analyzed during this study are available from the corresponding author and first author upon reasonable request.

Ethics statement

The study is in conformity with the French bioethics and clinical research and data legislation protection: Order no 2017-884 of 9 May 2017 modifying some regulatory dispositions relative to research involving human beings. *Official Journal of French Republic*, 10 May 2017, Text 84 on 396[1].

Informed consent statement

Written informed consent was obtained from all individual participants or their guardians included in the study. Furthermore, the systematic use of video recordings during developmental and diagnostic assessments of the child was subject to written consent from the families.

CRediT authorship contribution statement

Jean-Louis Adrien: Conceptualization, Methodology, Validation, Investigation, Data curation, Writing - review & editing, Supervision, Project administration. **Emmanuelle Taupiac:** Conceptualization, Methodology, Validation, Investigation, Writing - original draft, Resources. **Eric Thiébaut:** Methodology, Software, Validation. **Marie-Anna Paulais:** Methodology, Investigation, Resources, Writing - original draft. **Julien Van-Gils:** Investigation, Resources. **Kelley Kaye:** Methodology, Investigation, Writing - review & editing, Resources. **Romuald Blanc:** Methodology, Investigation, Writing - review & editing, Resources. **Maria Pilar Gattegno:** Methodology, Investigation, Writing - review & editing, Resources. **Yves Contejean:** Methodology, Investigation, Resources, Writing - review & editing. **Grégory Michel:** Conceptualization, Methodology, Investigation, Supervision, Project administration. **Annika Dean:** Writing - review & editing. **Catherine Barthélémy:** Methodology, Resources, Investigation. **Didier Lacombe:** Conceptualization, Methodology, Investigation, Supervision, Project administration, Writing - review & editing.

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