

Language regression in autism spectrum disorder: a systematic review

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Abstract: A significant portion of children with Autism Spectrum Disorder (ASD) is affected by the loss of language skills. This study's objective was to systematically review papers addressing this phenomenon characterizing the loss of skills in ASD. Bibliographic references were systematically searched in five databases: PubMed, Web of Science, PsycINFO, Lilacs and Scielo. Two independent judges selected and extracted data. The search resulted in 30 studies. Language regression tended to occur around 24 months of age and was generally accompanied by the loss of other skills. Beginning in 2000, studies in the field became more frequent, with a refined operational definition of the phenomenon. Important gaps were identified and can motivate the development of future studies, such as a lack of prospective studies and the need to discuss the conceptual definition of developmental regression.

Key words: autistic disorder; child development; regression; language; review.

REGRESSÃO DE LINGUAGEM NO TRANSTORNO DO ESPECTRO AUTISTA: UMA REVISÃO SISTEMÁTICA

Resumo: Uma parcela importante de crianças com Transtorno do Espectro Autista (TEA) é acometida pela perda de habilidades de linguagem. Esse estudo objetivou revisar sistematicamente as publicações sobre tal fenômeno, caracterizando a perda de habilidades no TEA. Foi realizada uma busca sistemática de referências bibliográficas em cinco bases de dados: PubMed, Web of Science, PsycINFO, Lilacs e Scielo. A seleção e a extração dos dados foram realizadas por dois juízes independentes. A busca resultou em 30 estudos, uma vez que o início da regressão de linguagem tendeu a ocorrer em torno dos 24 meses de vida da criança, geralmente acompanhada por perda de outras habilidades. Os estudos nesta área tornaram-se mais frequentes a partir dos anos 2000, sendo a definição operacional do fenômeno refinada. Foram identificadas lacunas importantes para o desenvolvimento de novas pesquisas, como a carência de estudos prospectivos e a necessidade de discussões acerca da definição conceitual da regressão desenvolvimental.

Palavras-chave: Transtorno autístico; Desenvolvimento infantil; Regressão; Linguagem; Revisão.

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REGRESIÓN DE LENGUAJE EN EL TRASTORNO DEL ESPECTRO AUTISTA: UNA REVISIÓN SISTEMÁTICA

Resumen: Un número significativo de niños con Trastorno del Espectro Autista (TEA) es acometido por la pérdida de habilidades de lenguaje. Este estudio objetivó revisar sistemáticamente la literatura sobre tal fenómeno, detallando la pérdida de habilidades no TEA. Se realizó una búsqueda sistemática de referencias en cinco bases de datos: PubMed, Web of Science, PsycINFO, Lilas y Scielo. La selección y extracción de datos fueron realizadas por dos jueces independientes. La búsqueda resultó en 30 estudios, siendo que el inicio de la regresión de lenguaje ha ocurrido alrededor de los 24 meses de vida del niño, generalmente acompañada por la pérdida de otras habilidades. Los estudios en esta área se volvieron más frecuentes a partir de los años 2000, siendo la definición operacional del fenómeno refinada. Se identificaron lagunas importantes para el desarrollo de nuevas investigaciones, como la carencia de estudios prospectivos y la necesidad de discusiones acerca de la definición conceptual de la regresión del desarrollo.

Palabras clave: trastorno autístico; desarrollo infantil; regresión; lenguaje; revisión.

Introduction

Individuals with Autism Spectrum Disorder (ASD) present social communication disorders, in addition to repetitive and stereotyped behavior, though the presentation and symptoms vary (American Psychiatric Association [APA], 2013). Likewise, both the nature of ASD and the age when its first signs appear vary among individuals (Zanon, Backes, & Bosa, 2014), as well as how the disorder progresses (Zwaigenbaum, Bryson, & Garon, 2013).

Zwaigenbaum *et al.* (2013) hold that ASD may begin early, in which symptoms become apparent in the first year of life, or be regressive, in which symptoms are preceded by a period of an apparently typical, development and then followed by a loss of skills previously acquired. There is no consensus, however, whether development attained before the loss of skills is typical, or delays and behavioral changes could have been observed but were missed. Thus, some individuals with ASD present developmental regression (DR) defined as definitive or significant loss of previously acquired skills (Baird *et al.*, 2008; Meilleur & Fombonne, 2009).

One meta-analysis addressed, among other factors, the prevalence, and age when loss of skills take place in ASD (Barger, Campbell, & McDnough, 2013). The authors reviewed 85 papers that represented 29,035 participants with ASD. The weighted mean indicated a prevalence rate of RD of 32.1% and the mean age when losses began was 21.36 months; the last information was based on 24 studies (Barger *et al.*, 2013). Note that the prevalence of DR may vary according to the operational definition of regression, the way it is assessed, and the sample under study (e.g., clinical, survey). In general, however, the loss of skills is a phenomenon that affects a significant number of children with ASD.

Studies show that DR may concomitantly affect different areas of development, resulting in loss of language skills, social interaction and the ability to play (Backes *et al.*, 2013; Baird *et al.*, 2008; Castillo *et al.*, 2008; Jones & Campbell, 2010; Lord, Schulman,

& DiLavore, 2004; Luyster *et al.*, 2005; Meilleur & Fombonne, 2009; Tamanaha, Machado, Loebmann, & Perissinoto, 2014; Thurm, Manwaring, Luckenbaugh, Lord, & Swedo, 2014). Explanation for the concomitant occurrence of loss of language, social interaction skills and the ability to play is based on the socio-pragmatic approach in which the acquisition of language is linked to socio-cognitive and socio-interactive bases; that is, the emergence of the linguist symbols (i.e., words) takes place after establishing social and cognitive skills during social interaction (Tomasello, 1999/2003). Hence, the process of symbolism production permeates the development of language and children's play and occurs in social exchanges (Tomasello, 1999/2003). Hence, language, social interaction and play are correlated developmental areas.

Note that language regression, more specifically the loss of words, and not the loss of other skills, tends to be characteristic among children with ASD, in contrast with other conditions, such as the Landau-Kleffner syndrome (Lord *et al.*, 2004; Pickles *et al.*, 2009; Shinnar *et al.*, 2001; Valente & Valério, 2004; Wilson, Djukic, Shinnar, Dharmani, & Rapin, 2003), and this is the focus of this study. Considering a lack of consensus regarding the conceptual definition of language regression, it has been operationally defined, based on the measures used. These measures include the Autism Diagnostic Interview-Revised (ADI-R), an instrument considered to be the gold standard for the diagnostic assessment of ASD. This instrument operationally defines language regression as the loss of communicative (spontaneous) use of three to five words, except for of "papa" and "mama" (Lord, Rutter, & LeCouteur, 1994). Additionally, ADI-R uses two time-parameters that refer to a period equal to or longer than three months, one of which is the period before the loss (i.e., period in which words previously learned were used communicatively) and the other is the duration of loss (i.e., time during which the child did not use the words lost). For this reason, in this study, we use the term 'loss of words'. Some studies report oral language as the skill most commonly affected by RD; loss of words occurs in approximately 20% of the individuals with ASD (Backes *et al.*, 2013; Lord *et al.*, 2004).

In this sense, we consider 'word' the linguistic symbol that consistently represents a given object or event, even if its form of presentation (or structure) differs from the conventional use but is close to the model provided to the child (e.g., 'eat' instead of 'food', 'woof-woof' instead of 'dog'). Obviously, one is not neglecting the different facets of oral language acquisition, which involves various complexities, such as inferring different meanings of linguistic symbols, grammatical categorization and understanding potential linguistic constructions related to certain words (Clark, 2012). Acquisition of the first words, however, occurs when children began to understand the meaning assigned to them, in general beginning at the end of the first year of life (Clark, 2012).

Note that language regression, and more specifically, the loss of words, has been highlighted as a potential early indicator of ASD for that subgroup whose onset pattern might be termed a "regressive start" (APA, 2013; Lord *et al.*, 2004). This is due to the fact this loss more frequently occurs among children with ASD, as some comparative

studies, using controls with Down Syndrome and specific language disorder, report (Pickles *et al.*, 2009; Shinnar *et al.*, 2001; Thurm *et al.*, 2014; Wilson *et al.*, 2003).

Nonetheless, despite the apparent importance of linguistic regression, and more specifically loss of words, both regarding diagnosis and intervention, this phenomenon remains unclear, which results in a lack of specific preventive and therapeutic measures. Additionally, results of studies in the field vary greatly. To clarify the heterogeneity of findings in the field of language regression, and therefore, to understand better the phenomenon itself, some questions need to be considered. For how long has language regression been studied? How has it been defined and investigated? Are there factors that can explain the occurrence of this phenomenon? Is it an isolated factor or is it accompanied by the loss of other skills? How did language develop before its loss? Because it is a still expanding field of research, these (and many other) questions remain unanswered. In an attempt to find the answers to such questions, this study was designed to provide tools for professionals, clinicians, and scholars, as well as to identify the occurrence and characteristics of language regression, more specifically the loss of words in the population with ASD. Note that, even though reviews addressing DR in ASD have been conducted, no systematic literature reviews were found specifically focusing on language regression.

Therefore, this study's objective was to systematically review studies addressing language regression in ASD, characterizing the loss of skills in this population (i.e., definition of the phenomenon, measures to investigate language regression, age when loss takes place, duration of loss, associated factors, co-occurrence with the loss of other abilities), focusing on the loss of words. Additionally, this study presents information regarding the development of language prior to its loss, whenever such information is available.

Method

Material analysis

Papers addressing language regression in ASD were included. A search was conducted in Brazilian and international databases, considering studies published up to February 17th, 2016. No chronological restriction was established, and papers written in Spanish, English, Portuguese or French from 1985 to 2014 were analyzed.

Procedures

Bibliographic references were searched in five electronic databases: PubMed, Web of Science, PsycINFO, Lilacs, and Scielo. The following descriptors were used in the Brazilian databases: "*autismo*" OR "*transtornos globais do desenvolvimento*" AND "*regressão*" OR "*perda*" AND "*linguagem*" while their equivalents were searched in international databases: "*autism*" OR "*pervasive developmental disorder*" AND

“regression” OR “setback” AND “language”. The terms “autism” and “regression” and “language” were cross-referenced, then “autism” and “loss” and “language”, and so on until all possibilities were exhausted, which resulted in four combinations per language. We performed only one search per database using the Boolean OR because, depending on the database, it is less precise in comparison to searches using AND.

The initial inclusion of papers was based on their abstracts, while the application of exclusion criteria and data extraction was based on the full texts. Two independent judges (this study’s authors) performed both procedures (selection and extraction). One expert with recognized clinical and academic experience in this field was consulted whenever the judges disagreed in regard to the studies to be selected or information collected in order to reach consensus. Inter-judge agreement in regard to the final selection of studies was 72.6%. Empirical studies addressing aspects related to the loss of skills among individuals with ASD were initially included. Based on the full texts, the following were excluded: (1) studies that involved only children with conditions other than ASD (e.g., Rett syndrome, Fragile X syndrome, Landau-Kleffner syndrome); (2) studies that did not address language regression; and (3) studies that did not characterize the loss of language skills. In regard to this last criterion, characterization of loss of language was operationally defined as presenting two or more of the following: age when loss started, duration of loss, association with external factors (e.g., fever, convulsions, stressful events), co-occurrence of loss of other skills (e.g., social interaction skills, ability to play or practice self-care). Characterization of the sample with language regression (e.g., mean age, scores of diagnostic instruments, intelligence quotient) was not considered in criterion 3. Also, note that studies, the full texts of which were not available in the database, were excluded after directly requesting them of the authors and/or periodicals and receiving no response. Figure 1 presents the flowchart concerning the selection of papers.

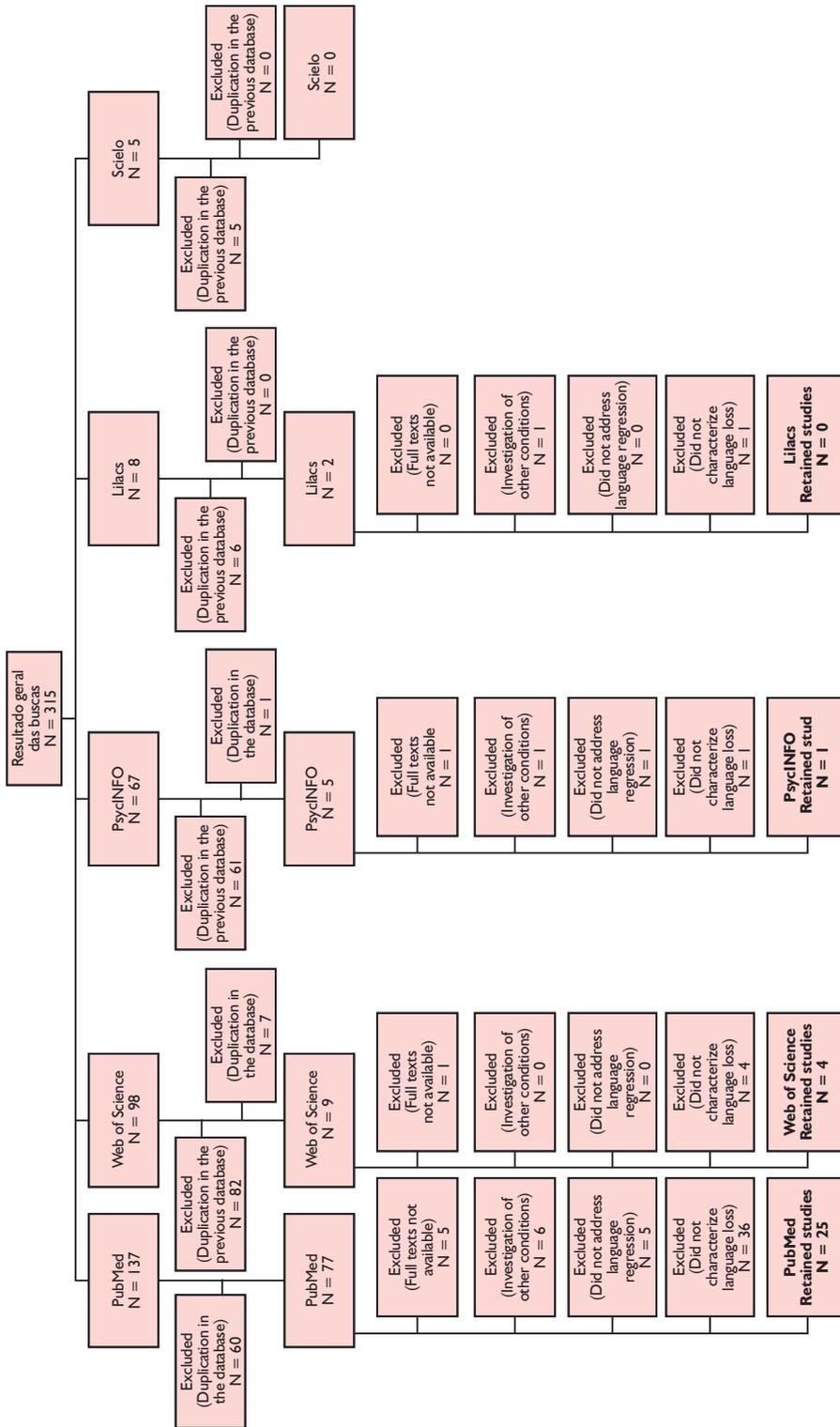
Information analysis

The selected studies were initially characterized according to objectives, participants, periodical and year of publication. Additionally, information concerning language regression was selected according to data available in each study, that is, definition and instrument used to investigate the phenomenon, mean age, and date of loss, mean duration of loss, association with health or family problems, and co-occurrence with the loss of other abilities. Finally, information concerning language development before loss took place is also presented, when available.

Results

Thirty out of the 315 studies initially selected met the inclusion and composed the corpus of this review. The complete references of the selected studies are highlighted

Figura 1. Flowchart of Studies Selection.



Source: Developed by the authors.

with an asterisk (*) in the list of references. Table 1 presents the characterization of the studies, including authors, objective, number of participants and ages, year and periodical. The studies were published between 1985 and 2014; the number of participants ranged from one to 585; and the studies encompassed various objectives, most of which focused on regression. Additionally, 86.6% ($n = 26$) of the studies were published in North American or European journals, the remaining in Brazilian ($n = 2$) and Asian journals ($n = 2$).

Table 1. Characterization of the 30 Studies Selected in Alphabetical Order according to Author.

No.	Authors (Year)	Study's objective	Number of participants (Mean age and Standard Deviation)	Periodical
1	Backes, Zanon, & Bosa (2013)	To investigate the relationship between oral language regression and socio-communication development among children with ASD	30 children: 6 with regression (M = 4.83 years old; SD = 0.33) and 24 without regression (M = 3.91 years old; SD = 0.15)	CoDAS
2	Baird, Robinson, Boyd, & Charman (2006)	To perform electroencephalographic sleep analysis in children with autism with and without regression	64 children: 39 with and 25 without regression (M = 35.6 months old; SD = 8.2)	Developmental Medicine & Child Neurology
3	Baird et al. (2008)	To investigate the nature and characteristics associated with regression among children with autism, with other global developmental delay (GDD) and other neurodevelopmental disorders (without ASD)	255 children: 53 with autism; 105 with GDD; and 97 with other neurodevelopmental disorder (M = 12 years old, SD = 1.1)	Journal of Autism and Developmental Disorders
4	Bernabei, Cerquiglini, Cortesi, & D'Ardia (2007)	To verify potential differences in the development of children with autism, with and without regression	40 children (M = 35.2 months old; SD = 8.9 months old): 18 with and 22 without regression	Journal of Autism and Developmental Disorders
5	Canitano & Zapella (2006)	To discuss the clinical characteristics, therapeutic approaches, and potential consequences of autistic epileptiform regression	One boy (NR) and one girl (4.5 years old)	Functional Neurology

(to be continued)

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No.	Authors (Year)	Study's objective	Number of participants (Mean age and Standard Deviation)	Periodical
6	Castillo <i>et al.</i> (2008)	To compare regression among children with autism, with and without Down syndrome	12 children with autism and Down syndrome (M = 9.8 years old; SD = 3.8) and 12 children with autism without Down syndrome (M = 9.2 years old; SD = 3.2)	Journal of Developmental & Behavioral Pediatrics
7	Chilosi <i>et al.</i> (2014)	To describe the case of a boy with autism and language regression	One boy (25 months old)	Journal of Child Neurology
8	Christopher, Sears, Williams, & Hersh (2004)	To revise the medical and family conditions of children with autism, with and without regression	51 children with autism without regression (M = 4.39 years old; SD = NR), 31 children with autism and regression (M = 4.71 years old; SD = NR)	Journal of Developmental and Physical Disabilities
9	Ekinci, Arman, Melek, Bez, & Berkem (2012)	To investigate the association of medical, developmental and psychiatric variables with autistic regression and its subtypes	57 children with ASD (M = 83 months old; SD = 36.3)	European Child & Adolescent Psychiatry
10	Goldberg <i>et al.</i> (2003)	To present an instrument that assesses the characteristics of regression	44 children with ASD (M = 6.06 years old; SD = 2.75)	Journal of Autism and Developmental Disorders
11	Hansen <i>et al.</i> (2008)	To present the prevalence of DR in ASD and investigate association between type of ASD onset and clinical and demographical factors and adaptive and developmental functioning	333 children with ASD (M = 44 months old; SD = 10)	Ambulatory Pediatrics
12	Jones & Campbell (2010)	To investigate the clinical characteristics of language regression and plateauing in children with ASD	114 children (M = 41.4 months old; SD = 9.3)	Journal of Autism and Developmental Disorders

(to be continued)

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No.	Authors (Year)	Study's objective	Number of participants (Mean age and Standard Deviation)	Periodical
13	Kobayashi & Murata (1998)	To perform a retrospective analysis of the relationship between regression and prognosis over the long term in a group of individuals with autism	179 individuals (M = 21.9 years old; SD = 3.2)	Acta Psychiatrica Scandinavica
14	Kumar, Karmakar, & Mohanan (2014)	To describe language regression in children later diagnosed with ASD and determine the age at which regression occurred	30 children with ASD (M = 64.5 months old; SD = NR)	International Journal of Pediatric Otorhinolaryngology
15	Kurita (1985)	To investigate the occurrence of loss of language in children with autism and describe the characteristics of this phenomenon	261 children with autism: 97 with word loss (M = 5.1 years old; SD = NR) and 164 without loss of words (M = 5.2; SD = NR)	Journal of the American Academy of Child Psychiatry
16	Kurita, Kita, & Miyake (1992)	To compare clinical characteristics of children with disintegrative psychosis and childhood autism with and without loss of language	18 children with disintegrative psychosis (M = 6.4 years old; SD = 2.7) and 196 with autism (M = 7.4 years old; SD = 3.6); 51 with loss of language and 145 without loss of language	Journal of Autism and Developmental Disorders
17	Lord, Shulman, & DiLavore (2004)	To investigate word loss in children at risk of autism, with developmental delay, and typical development	110 children with autism (up to 24 months old), 21 with developmental delay (up to 24 months old) and 33 with typical development (between 20 and 32 months old)	Journal of Child Psychology and Psychiatry
18	Luyster <i>et al.</i> (2005)	To investigate the characteristics and potential consequences of regression in the socio-communicative development of children with ASD	351 children with ASD (M = 9.64 years old; SD = 2.68), 21 with developmental delay (M = 12.68 years old; SD = 0.9) and 31 with typical development (M = 8.53; SD = 2.8)	Developmental Neuropsychology

(to be continued)

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No.	Authors (Year)	Study's objective	Number of participants (Mean age and Standard Deviation)	Periodical
19	Malhi & Singhi (2012)	To investigate the characteristics of autistic regression, comparing between children with ASD with and without DR	35 children with ASD and DR (M = 3.47 years old; SD = 0.93) and 35 children with ASD but without DR (M = 3.63 years old; SD = 1.56)	Indian Journal of Pediatrics
20	McVicar, Ballaban-Gil, Rapin, Moshé, & Shinnar (2005)	To investigate the relationship between epileptiform abnormalities and language regression in children with ASD	149 children with ASD (NR): 46 with language regression and 103 with autistic regression and language regression	Neurology
21	Meilleur & Fombonne (2009)	To compare the symptomatology of children with ASD, with and without regression	135 children with ASD (M = 6.3 years old; SD = 4.1)	Journal of Intellectual Disability Research
22	Nizamie, Sengupta, Mishra, Praharaj, & Nizamie (2010)	To present a case of autistic regression that responded well to both pharmacological and behavioral interventions	One girl (4 years old)	Acta Neurologica Taiwanica
23	Parr <i>et al.</i> (2010)	To investigate the characteristics of DR in children with ASD	458 children with ASD (M = 105, 8 months old; SD = NR)	Journal of Autism and Developmental Disorders
24	Pickles <i>et al.</i> (2009)	To investigate the incidence of loss of language in autism and specific language disorder	313 children (NR)	Journal of Child Psychology and Psychiatry
25	Shinnar <i>et al.</i> (2001)	To describe the clinical characteristics of children with a history of language regression	177 children (NR)	Pediatric Neurology
26	Shumway <i>et al.</i> (2011)	To investigate the proportion of children whose ASD appeared early and with language regression	272 children with ASD (M = 43.7 months old; SD = 14.9)	Journal of Autism and Developmental Disorders
27	Tamanaha, Machado, Loebmann, & Perissinoto (2014)	To compare the attainment and development of speech in children with ASD with and without autistic regression	64 children with ASD (between 3 and 10 years old)	CoDAS

(to be continued)

Table 1. Characterization of the 30 Studies Selected in Alphabetical Order according to Author.

No.	Authors (Year)	Study's objective	Number of participants (Mean age and Standard Deviation)	Periodical
28	Thurm, Manwaring, Luckenbaugh, Lord, & Swedo (2014)	To investigate the attainment and loss of socio-communicative skills in children with autism, global development disorder without any other specification, development delay and typical development	125 children with autism (M = 48.6 months old; SD = 16.9), 42 with GDD without any other specification (M = 48 months old; SD = 15.7), 46 with development delay (M = 43.3 months old; SD = 11.5) and 31 with typical development (M = 52.4 months old; SD = 17.8)	Development and Psychopathology
29	Tuchman & Rapin (1997)	To investigate the relationship between autistic regression and epilepsy	585 children with ASD (M = 70 months old; SD = NR)	Pediatrics
30	Wilson, Djukic, Shinnar, Dharmani, Rapin (2003)	To describe the characteristics, associated factors and consequences of language regression	196 children with language regression (M = 50.6 months old; SD = 41.1)	Developmental Medicine & Child Neurology

NR. Not reported/investigated.

Source: Developed by the authors.

A total of 86.6% (n=26) of the studies presented the operational definition used to investigate language regression and 43.3% (n = 13) used the ADI-R. Age at the beginning of language regression was available in 93.3% (n = 28) of the papers, ranging from 12 to 42 months. Information concerning the duration of loss could be analyzed only in 23.3% (n = 7) of the studies. Table 2 presents characterizations of language regression according to data available in each study, that is, the definition and instrument used to investigate the phenomenon, mean age when loss initiated, and mean duration of loss.

Table 2. Characterization of Language Regression According to Studies Organized by Authors' Alphabetic Order (N = 30).

Author (Year)	Operational definition of language	Instrument used to investigate language regression	Prevalence of language regression in ASD	Mean age of language regression onset (SD)	Mean duration of language regression duration (SD)
Backes et al. (2013)	Loss of communicative use of at least five words, except for 'papa' and 'mama' for a minimum period of three months	ADI-R	20%	25 months old (SD = 6.19)	16.3 months (SD = 4.24)
Baird et al. (2006)	Loss of communicative use of at least five words, with the exception of 'papa' and 'mama' for a minimum period of three months	ADI-R	51.6%	19.9 months old (SD = 5.2)	NR
Baird et al. (2008)	Loss of communicative use of at least five words, with the exception of 'papa' and 'mama' for a minimum period of three months	ADI-R	30.2% in the group with autism and 8% in the group with GDD	25 months old (SD = 1.5)	NR
Bernabei et al. (2007)	Loss of communicative use of at least five words, with the exception of 'papa' and 'mama' for a minimum period of three months	Semi-structured interview administered to parents and viewing home videos	NR	20.6 months old (SD = 3.8)	NR
Canitano & Zapella (2006)	Progressive loss of previously acquired language skills	NR	NR	Girl: 41 months old Boy: 24 months old	Girl: 17 months old Boy: 65 months old
Castillo et al. (2008)	Loss of communicative use of at least five words, with the exception of 'papa' and 'mama' for a minimum period of three months	ADI-R	NR	Group with autism and without Down Syndrome: 19.7 months old (SD = 5.8)	NR
Chilosi et al. (2014)	NR	Interview with parents	NR	20 months old	6 months old

(to be continued)

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Author (Year)	Operational definition of language	Instrument used to investigate language regression	Prevalence of language regression in ASD	Mean age of language regression onset (SD)	Mean duration of language regression duration (SD)
Christopher <i>et al.</i> (2004)	Loss of the consistent use of at least one word used to refer to a person or object	Interview with parents	NR	18.96 months old	NR
Ekinci <i>et al.</i> (2012)	Clear loss of at least five words for at least three months before 30 months of age	Interview, medical records and videos, whenever available	NR	NR	NR
Goldberg <i>et al.</i> (2003)	Loss, for at least three months, of the consistent and spontaneous use of isolated words or simple phrases used for at least three months before loss	ADI-R and Regression Supplement Form	NR	M = 20.69 months old (SD = 6.38), in the group with the loss of at least five words (n = 23)	NR
Hansen <i>et al.</i> (2008)	Loss of communicative use of at least five words, except for 'papa' and 'mama', for at least three months	ADI-R	33.9%	NR	NR
Jones & Campbell (2010)	Period of normal development, reinforced by the attainment of at least one verbal milestone at the expected age (e.g., isolated words at 2 years old) and report of definitive loss of these skills during childhood (typically followed by significant delay in language and/or evidence of aberrant speech frequently associated with autism)	ADI-R, parents' interviews and/or assessment reports	29.8%	M = 19.5 months old (SD = 6.9)	NR

(to be continued)

Table 2. Characterization of Language Regression According to Studies Organized by Authors' Alphabetic Order (N = 30).

Author (Year)	Operational definition of language	Instrument used to investigate language regression	Prevalence of language regression in ASD	Mean age of language regression onset (SD)	Mean duration of language regression duration (SD)
Kobayashi & Murata (1998)	Regressive changes affecting a child's global development for a minimum period of three months, including loss of words used at the beginning of childhood, accompanied by a loss of interest in the outer world even though normal development (or close to typical development) was attained before the loss	Parents' interview	29.6%	NR	NR
Kumar <i>et al.</i> (2014)	NR	Parents' interview based on a screening questionnaire for regression	NR	M = 19.16 months old (NR)	NR
Kurita (1985)	Loss, before 30 months of age, of all words said spontaneously in a situation and the child should not use words for at least six months	Records of speech therapists and psychologists, and questionnaire applied to the parents	37.2%	M = 18 months old	NR
Kurita <i>et al.</i> (1992)	Loss of all words said spontaneously in a situation and the child should not use words for at least six months	Records of speech therapists and psychologists	NR	M = 16 months old (SD = 3.6)	NR
Lord <i>et al.</i> (2004)	Loss, for at least one month, of at least three words used daily and spontaneously for at least one month	ADI-R	25%	M = 16.2 months old (SD = 3.63)	M = 4.67 months old (SD = 3.38)
Luyster <i>et al.</i> (2005)	Loss, for at least one month, of at least three words used daily and spontaneously	ADI-R	35.6%	M = 18.50 months old (SD = 5.34)	NR

(to be continued)

Table 2. Characterization of Language Regression According to Studies Organized by Authors' Alphabetic Order (N = 30).

Author (Year)	Operational definition of language	Instrument used to investigate language regression	Prevalence of language regression in ASD	Mean age of language regression onset (SD)	Mean duration of language regression duration (SD)
Malhi & Singhi (2012)	NR	Parents' interview	NR	Entre 18 e 24 months old	NR
McVicar et al. (2005)	Loss of language skills after attaining a vocabulary of at least five words.	Clinical records	NR	M = 25.7 months old (SD = 16.7) in the group with autistic and language regression	NR
Meilleur & Fombonne (2009)	Loss, for at least three months, of the communicative use of at least five words used daily for at least three months	ADI-R	9.6%	M = 24.4 months old (SD = 9.4)	M = 20.9 months old (SD = 14.9)
Nizamie et al. (2010)	NR	Parents' interview	NR	Between 18 and 24 months old	NR
Parr et al. (2010) ¹	Loss of communicative use of at least five words for a minimum period of three months before the age of 36 months old	ADI-R	10.2%*	M = 23.2 months old (SD = 7.2) ¹	M = 23.2 months old (SD = 20.4) ¹
Pickles et al. (2009)	Loss of communicative use of at least five words used for at least three months before the loss	ADI-R	15%	Between 12 and 33 months old	NR
Shinnar et al. (2001)	Loss of language skills previously acquired, with normal development or developmental delay before the loss	Clinical records	NR	M = 22.8 months old (NR) ²	NR
Shumway et al. (2011)	Loss of communicative use of at least five words for a minimum period of three months	ADI-R	NR	NR	NR

(to be continued)

Table 2. Characterization of Language Regression According to Studies Organized by Authors' Alphabetic Order (N = 30).

Author (Year)	Operational definition of language	Instrument used to investigate language regression	Prevalence of language regression in ASD	Mean age of language regression onset (SD)	Mean duration of language regression duration (SD)
Tamanaha <i>et al.</i> (2014)	Cessation of the production of speech after the acquisition of at least five words	Parents' interview	32%	24 months old (SD = 8.43)	NR
Thurm <i>et al.</i> (2014)	Substantial loss of the communicative use of words used for at least one month before the loss	Regression Validation Interview-Revised	47% in the group with autism and 32% in the group with GDD without any other specification	Group with autism: M = 21 months old (SD = 1.0) Group with GDD without any other specification: M = 18.7 months old (SD = 2.1)	NR
Tuchman & Rapin (1997)	Loss of the communicative use of at least three words for a minimum period of three months	Parents' report	30%	M = 21 months old (NR)	NR
Wilson <i>et al.</i> (2003)	Loss of previously acquired language skills, with or without developmental delay before the loss	Parents' report	NR	M = 21.2 months old (SD = 10.5) ²	M = 13.4 months old (NR)

NR. Not reported/investigated.

Source: Developed by the authors.

Additionally, 76.6% (n = 23) of the studies investigated the relationship between language regression and health problems, while 73.9% (n = 17) of these analyzed aspects that concerned electroencephalographic alterations or a history of convulsion. On the other hand, only 23.3% (n = 7) of the studies investigated the relationship with family problems or stressful events, and all depended on the parents' reports. Of the 22 studies that found language regression concomitantly with the loss of other abilities, 90.1% (n = 20) reported the loss of social interaction and/or playing abilities. Table 3 presents this information in detail.

Table 3. Co-occurrence of Language Regression with Health Problems, Family Problems, and Loss of other Skills, According to Study Organized by Authors' Alphabetical Order (n = 28).

Author (Year)	Relationship between language regression in ASD and health problems/diseases (investigated aspects)	Relationship between language regression in ASD and family problems or stressful events (investigated aspects)	Co-occurrence of language regression with the loss of other skills (co-occurrence skills)
Backes <i>et al.</i> (2013)	No (organic diseases) ¹	NR	Yes (social interaction skills)
Baird <i>et al.</i> (2006)	No (epileptiform electroencephalograms)	NR	Yes (social interaction and non-verbal communication skills)
Baird <i>et al.</i> (2008)	No (gastrointestinal problems or epilepsy)	NR	Yes (social interaction, imaginative play, motor and movement skills)
Bernabei <i>et al.</i> (2007)	No (cranial circumference)	NR	Yes (unspecified)
Canitano & Zapella (2006)	Yes (epileptiform discharge in centrotemporal regions)	NR	Yes (social interaction and play skills)
Chilosi <i>et al.</i> (2014)	Yes (focal EEG abnormalities)	NR	Yes (social interaction skills)
Christopher <i>et al.</i> (2004)	No (family history of disorders or diseases, pre- or perinatal factors, or medical conditions)	NR	NR
Ekinci <i>et al.</i> (2012)	Yes (Sleep disorders)	NR	NR
Goldberg <i>et al.</i> (2003)	Yes (vaccination, diseases, medications) ¹	Yes (moving house) ¹	Yes (social interaction and play skills)
Hansen <i>et al.</i> (2008)	No (gastrointestinal problems, history of convulsions or sleep disorders)	NR	Yes (social interaction skills)
Jones & Campbell (2010)	No (history of convulsions)	NR	NR
Kobayashi & Murata (1998)	Yes (epilepsy)	Yes (stressful events such as maternal hospitalization, birth, and home moving) ¹	Yes (social interaction skills)

(to be continued)

Table 3. Co-occurrence of Language Regression with Health Problems, Family Problems, and Loss of other Skills, According to Study Organized by Authors' Alphabetical Order (n = 28).

Author (Year)	Relationship between language regression in ASD and health problems/diseases (investigated aspects)	Relationship between language regression in ASD and family problems or stressful events (investigated aspects)	Co-occurrence of language regression with the loss of other skills (co-occurrence skills)
Kumar <i>et al.</i> (2014)	NR	NR	Yes (social interaction and play skills)
Kurita (1985)	No (perinatal risk or paroxysmal EEG abnormalities)	Yes (stressful events, such as the birth of siblings) ¹	NR
Kurita <i>et al.</i> (1992)	Yes (not specified) ¹	Yes (not specified) ¹	Yes (use of the pointing gesture)
Lord <i>et al.</i> (2004)	No (convulsions, pre-, peri- and neonatal risk factors)	NR	NR
Luyster <i>et al.</i> (2005)	No (medical risk factors such as convulsion)	NR	Yes (social interaction and/or play skills)
Malhi & Singhi (2012)	Yes (medical diseases) ¹	Yes (maternal concerns about job and change of caregiver) ¹	Yes (social skills and other not specified)
McVicar <i>et al.</i> (2005)	Yes (convulsion)*	NR	Yes (unspecified autistic regression)
Meilleur & Fombonne (2009)	No (epilepsy or other organic diseases)	NR	Yes (social interaction and play skills)
Nizamie <i>et al.</i> (2010)	Yes (convulsion)	NR	Yes (social interaction skills)
Parr <i>et al.</i> (2010) ¹	NR	NR	Yes (social interaction, play, adaptive, motor and pre-academic skills)
Shinnar <i>et al.</i> (2001)	Yes (health problems such as convulsion and otitis) ^{1,2}	Yes (family problems, such as the birth of siblings and home moving) ^{1,2}	NR

(to be continued)

Table 3. Co-occurrence of Language Regression with Health Problems, Family Problems, and Loss of other Skills, According to Study Organized by Authors' Alphabetical Order (n = 28).

Author (Year)	Relationship between language regression in ASD and health problems/diseases (investigated aspects)	Relationship between language regression in ASD and family problems or stressful events (investigated aspects)	Co-occurrence of language regression with the loss of other skills (co-occurrence skills)
Shumway <i>et al.</i> (2011)	NR	NR	Yes (social interaction skills)
Tamanaha <i>et al.</i> (2014)	NR	NR	Yes (social interaction and play skills)
Thurm <i>et al.</i> (2014)	NR	NR	Yes (social interaction skills)
Tuchman & Rapin (1997)	No (epilepsy) Yes (Epileptiform abnormalities)	NR	Yes (social interaction skills)
Wilson <i>et al.</i> (2003)	Yes (medical diseases, hospitalization and convulsions) ¹	Yes (emotional stressors such as the birth of siblings and home moving) ^{1,2}	Yes (social interaction and play skills) ^{1,2}

NR. Not reported/investigated. ¹Information provided by parents or caregivers, not statistically tested.

Source: Developed by the authors.

Finally, information regarding language development, more specifically, the age when the first language milestones were achieved, was available in 43.3% (n = 13) of the papers. In regard to the age when the child's first words were spoken, (n = 13) it ranged from 11 to 41.2 months, while in 84.6% (n = 11) of these studies, children were aged between 11 and 14 months. Information regarding the age when children spoke their first phrases was available in six studies and involved the period between 18.8 and 59 months of age. Additionally, two studies investigated a number of words used by children before the loss of words, while one study reports an average of 5.2 words and another 6.33.

Discussion and Final Considerations

This systematic literature review focused on language regression in ASD, a phenomenon that is characteristic in a portion of children with the disorder; it appears less frequently in other disorders (APA, 2013; Lord *et al.*, 2004; Pickles *et al.*, 2009, Thurm *et al.*, 2014). Together, information gathered in this review reveals that

language regression in ASD has been a topic of growing interest among researchers in recent years. In this sense, note its operational definition has been refined, since criteria currently used involve temporal parameters, both in regard to the use of the ability lost and the loss itself, in order to investigate the stability of these components (i.e., behavior and loss).

Studies began to address this phenomenon at least three decades ago, but most of the reviewed studies were developed after the 2000s. Williams, Brignell, Prior, Bartak and Roberts (2015) assert that research on DR in ASD has helped develop an understanding of the disorder and even its heterogeneity, though authors stress that this field still lacks information regarding the mechanisms implicated in the loss and its prognosis, for instance, while findings are very diverse.

The variability of results may be explained by different factors, such a lack of consensus concerning the conceptual definition of DR (Lampreia, 2013), which results in the use of different measures to investigate the phenomenon and different sampling methods (Barger *et al.*, 2013). In fact, the results of this study show considerable variability in the objectives, sample sizes, and to a less extent, in the instruments used to investigate language regression in ASD. In regard to this last aspect, the ADI-R was the measure most frequently used in the studies addressed here. The ADI-R is, however, a diagnostic interview that requires formal training, in addition to the fact it is privately owned. Therefore, in addition to not being an easily accessible instrument, it was not specifically developed to investigate regression, which probably motivated the development of other measures used in other studies such as the Regression Supplement Form (Goldberg *et al.*, 2003) and Regression Validation Interview-Revised (Thurm *et al.*, 2014). Additionally, as most of the studies addressed in this review are retrospective studies, some authors analyzed domestic videos to better understand the development of children before their linguistic loss, as well as the occurrence of the phenomenon itself (Bernabei *et al.*, 2007; Ekinci *et al.*, 2012). In fact, the use of domestic videos in the DR field, still seldom used, is promising because it also validates the reports of parents concerning such a loss. This validation is very relevant to the extent that, for some time, it was thought that DR was a parental "illusion", meaning that the affected children had never actually acquired the so-called lost skills. Hence, the analysis of domestic videos has attested to and clarified important aspects concerning the occurrence of this phenomenon.

This review also identified the operational definition of language regression used by the studies. Such a definition was used by most of the studies and tended to involve communicative loss of at least five words in a minimum period of three months and was clearly based on the way loss of abilities is investigated by the ADI-R (Lord *et al.*, 1994). This is, therefore, an examination of loss of words, and not the language itself, since the latter involves broader and more complex components. The concept of word implied in such an investigation is not discussed in the studies; that is, understanding of the configuration of this linguistic element (e.g., its form and structure) may not be

the same between researchers and parents, for instance. The way a word is used, on the other hand, tends to be addressed in the operational definition of language, since it involves loss of communicative use. In other words, it should not refer to the mere repetition of another person's speech, rather to symbolic elements used spontaneously in social interaction. Additionally, in order to examine the stability of loss, studies considered a period of time in which the phenomenon persisted, generally corresponding to three months. Together, different information shows that the operational definition of language regression involves different aspects that complement each other. Nonetheless, the issue related to a lack of consensus in the conceptual definition of this phenomenon remains. As highlighted by Lampreia (2013), it is imperative to consider the conception of regression in order to deepen scientific knowledge in the field and contribute to understanding ASD itself, considering that children affected by regression follow a developmental path within the spectrum (ASD) that contrasts with that followed by children who do not lose abilities, at the same time they share with each other characteristics that are inherent to the disorder.

In regard to the prevalence of language regression in ASD, data found in this study ranged from 9% to 51%, which may be explained by the different sampling methods used (Barger *et al.*, 2013), while the prevalence of language regression found in a meta-analysis developed by Barger *et al.*, 2013 was 24.9%. In regard to the age when loss took place, even though the interval was from 12 to 42 months, language regression after 30 months was reported only in two studies (Canitano & Zapella, 2006; Pickles *et al.*, 2009). In fact, research shows that DR tends to occur up to 30 months of age in ASD (Barger *et al.*, 2013), which contrasts with loss that occurs in Landau-Kleffner syndrome (LKS), also called acquired epileptic aphasia, in which loss of abilities tends to occur between 4 and 7 years of age (Valente & Valério, 2004). This information, however, is not sufficient to differentiate these two conditions because children tend to keep playing and maintain social interest while suffering from LKS, while the occurrence of repetitive movement is rare and there is also an association with abnormal electroencephalographic findings, such as idiopathic partial epilepsy (Valente & Valério, 2004). Unfortunately, most of the studies failed to provide information regarding the duration of loss. When such information was provided, it presented great variation. This may be explained by the difficulty in precisely establishing the age when abilities are acquired, since both acquisition and loss of abilities tend to be gradual (Malhi & Singhi, 2012).

The studies investigating the relationship between language regression and health problems used different analyses, from parents' reports up to statistical analysis of associations. In any case, most studies addressed aspects related to electroencephalographic changes, such as convulsions and epilepsy. This potential etiological factor was widely studied in the field of DR in ASD, but findings remain controversial (Williams *et al.*, 2015). Additionally, the few studies addressing the relationship between language

regression and stressful events were based on parents' reports, generally involving changes related to family routines (e.g., the birth of a sibling, moving house). The fact these children were later diagnosed with ASD, however, suggests that loss of abilities already constituted the developmental trajectory within the spectrum, and did not necessarily arise from stressors or changes in the children's families, situations considered potentially stressful events from an emotional point of view.

Most studies also report that language regression occurred concomitantly with the loss of other skills, especially the ability to socially interact and play. This result is in agreement with socio-interactionism and socio-cognitive notions of language acquisition (Tomasello, 1999/2003). Tomasello considers the acquisition of the first words to occur based on social-interaction experiences with caregivers during so-called dyadic (i.e., face-to-face interaction) and triadic situations (i.e., interaction mediated by objects) and constitutes the basis for the formation of symbolic capacity, expressed through speech and "make-believe" play. Therefore, from a conceptual point of view, it seems logical that a developmental rupture (or cessation) in any of these abilities affects correlates behaviors of this representational chain (symbolic). Nevertheless, this notion still leaves a question unanswered: how do we explain cases in which the loss of language does not occur concomitantly with the loss of other abilities? There are two possible explanations, both of a methodological nature. The first is related to the fact that most measures are based on parental reports. Thus, loss in other areas could be subtle to the point of not being perceived accurately, especially because the greatest concern of parents is focused on language alterations, more specifically, in speech delay (Zanon *et al.*, 2014). The other potential explanation concerns the measure most frequently used to examine the occurrence of regression, ADI-R, since it investigates language regression in more detail, which does not occur in regard to the loss of other abilities, such as those related to social interaction and play.

Finally, information on the linguistic development of children before the loss was available in less than half the studies. In most papers, the production of the first words took place around 12 months of age, suggesting these children had achieved this linguistic milestone within the expected age range (Clark, 2012). In regard to the age when first phrases emerged, among the four studies that report this information, only one found that children with language regression achieved this milestone within the expected age range (Clark, 2012), which may be related to the fact that the loss of words generally occurs around a child's second birthday (Barger *et al.*, 2013), a period when the first phrases emerge (Clark, 2012). In other words, such a loss could compromise acquiring this linguistic milestone. Considering the aspects previously presented, note that this review identified some gaps that can motivate other studies. Thus, future research addressing DR in ASD, more specifically addressing the loss of words, should verify the acquisition of abilities before such loss occurs to improve understanding regarding development prior to regression and the process of loss itself. Such aspects are especially relevant when one considers the role of language in

establishing the severity of ASD and its prognosis (APA, 2013). Note that the investigation of these aspects can be facilitated by analyzing home videos filmed before the loss, a procedure that the research group of which this review's authors are a part has adopted. Additionally, it is imperative that researchers expand discussions regarding the conceptual definition of DR and also of abilities (e.g., what is the concept of the word that should be adopted). Prospective research monitoring the development of children with ASD, with and without the loss of abilities, can significantly contribute to a better understanding of how regression progresses and its potential consequences. Therefore, studies addressing the efficiency of speech-language interventions among children with a history of language regression are potentially useful, especially from a therapeutic perspective. Finally, it is important to more deeply investigate the characteristics and socio-communicative performance of children with language regression who recovered their abilities. Together, these data can contribute to better understanding how this phenomenon occurs in ASD.

This study presents some limitations that should be addressed. For instance, only studies that characterized language regression were analyzed, while other studies addressing DR in ASD were excluded. Additionally, theoretical and systematic reviews were not included since this study's objective was to investigate empirical data. Finally, the descriptors may not have covered all related publications due to the possible use of different nomenclatures to designate language regression, for instance. Nevertheless, this study gathered a considerable amount of data in the field of language regression in ASD, indicating that children with a history of word loss may compose a subgroup within the spectrum. These results provide tools to professionals involved with child development in regard to the importance of the phenomenon, both regarding diagnostic investigation and interventions. In regard to the last aspect, we highlight the need for children to be referred to treatment as soon as the loss of abilities is perceived in order to minimize negative consequences of this phenomenon in child socio-communication development.

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