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Loss of Acquired Skills: Regression in Young Children With Autism Spectrum Disorders

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Objectives: Regression, while not a core symptom of autism spectrum disorder (ASD), has been suggested to be a distinct subtype by previous studies. Therefore, this study aimed to explore the prevalence and clinical differences between those with and without regression in children with ASD.

Methods: This study includes data from toddlers and young children aged 2–7 years acquired from other projects at Seoul National University Bundang Hospital. The presence and characteristics of regression were explored using question items #11–28 from the Autism Diagnostic Interview-Revised. Chi-square and independent t-tests were used to compare various clinical measurements such as autistic symptoms, adaptative behavior, intelligence, and perinatal factors.

Results: Data from 1438 young children (1020 with ASD) were analyzed. The overall prevalence rate of regression, which was mainly related to language-related skills, was 10.2% in the ASD group, with an onset age of 24 months. Regarding clinical characteristics, patients with ASD and regression experienced ASD symptoms, especially restricted and repetitive interests and behaviors, with greater severity than those without regression. Furthermore, there were significant associations between regression and hypertension/placenta previa.

Conclusion: In-depth surveillance and proactive interventions targeted at young children with ASD and regression should focus on autistic symptoms and other areas of functioning.

Keywords: Autism spectrum disorder; Regression; Clinical characteristics.

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INTRODUCTION

Autism spectrum disorder (ASD) is characterized by impairments in social communication, with restricted and repetitive patterns of behavior, interests, or activities (RRB) [1]. Regression is a phenomenon reported in children which entails a gradual or abrupt loss of previously acquired skills [2]. The Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision previously recommended diagnosing children with childhood disintegrative disorder (CDD) if they showed a period of "apparent normal development for at least the first 2 years" [3]. However, regression alone does not always signify CDD. Whether regression is a core ASD symptom remains controversial; however, there is a heightened interest in exploring regression in children with ASD. Review articles such as that by Tammimies [4] provide insight into how regression, similar to ASD, may have a strong genetic component and could therefore be regarded as an ASD subtype. As ASD has a broad spectrum, considering individuals with regression as a distinct subgroup may be vital to understanding the underlying etiology and the potential environmental factors.

The prevalence of regression in children with ASD varies from 8.33% [5] to 47.5% [6], depending on the definition of regression, sample population, and evaluation methods. While regression related to language skills is the most common form of developmental regression in individuals with ASD, studies have also observed regression in other areas of functioning [7,8]. The mean age of regression onset is approximately 15−30 months [9], with 42.86% of individuals regaining their skills after 19.5 months on average [5].

Studies have observed inconsistent clinical characteristics in terms of autistic symptoms or behavioral and psychological functioning in children with regression [5,10]. A study by Kim et al. [5], which explored regression in children with ASD, was conducted by the corresponding author's research team; they found significant differences in subdomain areas

of adaptive skills and verbal/nonverbal intelligence quotient scores. In contrast, a study by Malhi and Singhi [10] found no differences when comparing children with ASD with and without regression. Therefore, our study aimed to expand on the study by Kim et al. [5] with a larger sample size to determine whether the previous study findings can be generalized.

The study's main objectives are as follows: 1) to explore the prevalence of developmental regression in young children with and without ASD and 2) to investigate the types of regression reported in children with ASD and compare their clinical characteristics depending on the presence of regression.

METHODS

Participants

Data used in this retrospective study were acquired from various projects conducted at Seoul National University Bundang Hospital (SNUBH), including a genetic study to identify ASD-specific biomarkers and a project to validate a novel ASD screening instrument. Caregivers provided consent in each study for the retrospective use of the data. The Institutional Review Board of SNUBH approved the use of the fully anonymized data for analyses (IRB no; B-2210-784-104).

Participants aged 2–7 years were included. This age range was used to minimize parents' recall biases because the minimum age for applying the Autism Diagnostic Interview-Revised (ADI-R) is 24 months. Young children completed the gold-standard ASD diagnostic assessments and psychological evaluations while their caregivers filled out various questionnaires. The final diagnostic groups (ASD and non-ASD) were based on the best clinical estimate using all the procured clinical information.

Measures

ADI-R

The ADI-R [11,12] is a 93-item semi-structured caregiver interview to diagnose ASD. Questions are rated on the basis of current or past behaviors depending on participant age. Higher scores indicate greater symptom severity with selected items resulting in domain scores of social interactions, communication, RRBs, and symptom onset before 36 months.

Using the ADI-R, we defined regression as the loss of acquired language-related or other skills. Regression in language skills is the loss of skills in the spontaneous use of at least five meaningful words (#13), communicative intent (#14), syntactical skills (#15), and articulation (#16). Regression in other skills includes loss of purposive hand movements (#21), motor skills (#22), self-help skills (#23), imaginative play skills (#24), and social responsiveness (#25).

ASD-related assessments

The Autism Diagnostic Observation Schedule (ADOS) [13,14] is a diagnostic observation assessment. The calibrated severity scores were used to compare ASD severity across different modules. Questionnaires to measure autistic traits, such as the Korean-translated Social Communication Questionnaire [15] and Social Responsiveness Scale (SRS) [16], were completed by caregivers. Trained researchers scored the Childhood Autism Rating Scale (CARS) [17] using the obtained information from direct observations, caregiver interviews, and questionnaires. Higher scores implied greater symptom severity.

Other assessments

Additional information, such as adaptive behaviors, intelligence, and prenatal history, was collected to assist in the best diagnosis. Caregivers completed the second edition of the Vineland Adaptive Behavior Scale (VABS) [18] to measure adaptive functioning across communication, daily life, socialization, and motor skills. Intelligence was assessed using the Wechsler Preschool and Primary Scale of Intelligence [19] or the Wechsler Intelligence Scale for Children [20]. Young children with limited expressive language skills were administered the Leiter International Performance Scale [21]. We used age-matched standardized scores.

Data analyses

Regression was binarily coded on the basis of the ADI-R items. Prevalence of regression was calculated in both diagnostic groups, whereas characteristics of regression and clinical data were only compared among individuals with ASD. The chi-square test was performed to assess categorical variables such as sex and prenatal factors. Continuous clinical scores between those with and without regression were assessed with independent t-tests. Statistical analyses were conducted using SPSS version 26.0 (IBM Corp, Armonk, NY, USA).

RESULTS

A total of 1438 participants (1020 with ASD, 418 without ASD) aged 2–7 years were included in the analyses. Regression was reported in 10.2% of young children with ASD and 2.05% without ASD. Amongst the participants in the ASD group, no significant differences in sex or age were observed depending on the presence of regression (Table 1).

Of the young children with ASD, 77 had language skills-related regression, whereas 46 had regression related to other skills (Table 2). Nineteen participants experienced regression in both categories. The onset age of regression was approx-

Table 1. Demographic characteristics of young children with autism spectrum disorder (n=1020)

Characteristics	Regression (n=104)	No regression (n=916)	p-value
Sex			0.577
Male	82 (79.0)	743 (81.0)	
Female	22 (21.0)	173 (19.0)	
Age (months)	51.56±15.41	53.61±17.52	0.207

Data are presented as mean±standard deviation or n (%).

Table 2. Characteristics of regression in young children with autism spectrum disorder

Characteristics	Value
Classification of regression	
Regression related to language skills	77 (74.03)
- Spontaneous use of at least five meaningful words	62
- Communicative intent	55
- Syntactical skills (grammar)	0
- Articulation (pronunciation)	8
Regression related to other skills	46 (44.23)
- Purposive hand movements	9
- Motor skills	5
- Self-help skills	17
- Imaginative play skills	8
- Social responsiveness/ engagement	29
Both	19 (18.27)
Mean age at regression onset (months)	
Regression related to language skills	26.24±9.48
Regression related to other skills	24.22±10.13
Lost skills regained	
Regression related to language skills	46 (59.74)
Regression related to other skills	17 (36.96)
Duration of regression (months)	
Regression related to language skills	19.04±16.10
Regression related to other skills	22.35±15.34

Data are presented as mean±standard deviation or n (%).

imately 2 years. While 59.74% (n=46) of participants with language-related regression regained the skills after an average of 19.04 months, only 36.96% (n=17) of participants with regression in other skills regained function in the respective areas.

On comparing clinical characteristics between young children with and without regression in the ASD group, significant differences were observed in terms of autistic symptoms. Children with regression had higher scores in the RRB domains than those without, as measured using the ADOS (p=0.043) and ADI-R (p=0.028) assessments. CARS (p<0.001) and SRS T-scores (p=0.050) also showed greater ASD-related symptom severity in the regression group than in the non-regression group. Adaptive behaviors and psychological assessments also demonstrated a more significant developmental delay in young children with regression than in those without (Table 3).

Regarding the perinatal variables in the ASD group, regression was significantly associated with placenta previa (χ^2=9.48, p=0.002) and hypertension (χ^2=6.19, p=0.013).

DISCUSSION

Our findings demonstrate that the prevalence of developmental regression among young children with ASD (10.2%) is much higher than that among children without ASD (2.05%). Our findings align with the findings that regression occurs more frequently in the ASD group than in the non-ASD group [5]. A pooled estimate across four surveys found that the odds of CDD is 1.7 per 100000 (95% confidence interval: 0.6–3.8 per 100000) [22]. While the prevalence of regression among young children with ASD was slightly higher in our study than in that published in 2011 [5], a recent meta-analytic review [23] observed an overall regression rate of 32.1%.

Several factors could explain the wide range of prevalence rates. First, using the ADI-R to assess regression could have been biased by retrospective remembrance. Regression in young children with ASD was more prevalent in this study than in our previous one (8.3%) [5]. The former study excluded children <36 months of age; therefore, the participants in this study were older. Hence, regression may have been underreported by parents having to recall over an extended period. Second, cultural factors, which can affect the awareness of regression-related risk signs, could have played a role in how parents recall information. For example, in 1998, a study that was eventually retracted in 2010 [24] stated that developmental regression and gastrointestinal symptoms in ASD individuals could be precipitated by the Measles, Mumps, Rubella (MMR) vaccination. This study received enormous attention in Western countries. Consequently, MMR vaccination rates subsequently dropped owing to concerns regarding ASD risk after vaccination [25]. However, compared with the Western countries, in Korea, minimal attention was paid to this matter. Third, the definition of regression and assessment methods can affect the results. Several studies used simple surveys [6,26] based on small sample sizes. Fourth, there could be differences based on race or genetic factors. African-American children were twice as likely to have parent-reported regression than children of European descent whereas parents of Hispanic children were approximately 1.5 times more likely to report the early loss of skills [27]. Studies have reported the association of genetic factors with de-

Table 3. Clinical characteristics of young children with autism spectrum disorder

	Regression (n=104)	No regression (n=916)	p-value
ADOS			
Social affect CSS	7.54±1.75	7.56±1.67	0.921
RRB CSS	6.24±2.11	5.75±2.35	0.043
Total CSS	7.11±1.59	6.97±1.64	0.413
ADI-R			
Social interaction	19.32±6.16	18.25±6.02	0.088
Communication	12.51±5.94	13.43±4.96	0.193
RRB	5.62±2.40	5.05±2.48	0.028
Before 36 months	3.84±1.10	3.95±1.10	0.320
CARS	35.91±5.48	33.21±5.42	<0.001
SCQ			
Current	15.87±7.72	14.75±6.82	0.175
Lifetime	17.69±7.91	16.57±7.08	0.167
SRS T-score	71.23±14.56	67.85±11.98	0.050
VABS total score	59.39±12.44	68.38±23.93	0.041
Communication	62.36±14.25	71.51±18.52	0.001
Daily living skills	69.04±14.67	76.61±17.09	<0.001
Socialization	58.21±13.25	63.54±15.39	<0.001
Motor	73.30±12.30	78.16±14.24	0.002
IQ	64.86±12.94	76.76±21.38	0.041
Leiter	61.40±20.64	71.01±21.57	0.012

Data are presented as mean±standard deviation. ADOS, Autism Diagnostic Observation Schedule; CSS, calibrated severity score; RRB, restricted and repetitive behaviors; ADI-R, Autism Diagnostic Interview-Revised; CARS, Childhood Autism Rating Scale; SCQ, Social Communication Questionnaire; SRS, Social Responsiveness Scale; VABS, Vineland Adaptive Behavior Scale; IQ, intelligent quotient

velopmental regression in ASD individuals [28], suggesting that regression may be characteristic of a distinct subtype of ASD. Therefore, we urge researchers to investigate the underlying etiology and the potential association with observed clinical behaviors.

We observed that the prevalence of regression in the non-ASD group was higher than that in previously reported findings in the CDD population. This can be due to the inclusion of other developmental delays, such as delays in language or cognitive abilities. We were unable to further explore differences due to the limited number of participants who completed additional questionnaires or psychological assessments so as to evaluate other developmental delays.

Regarding regression types in children with ASD, language-related regression was higher (74.03%) than regression related to other skills (44.23%). Only 18.27% of the children reported having regression in both categories. Previous studies [5,10] also reported the loss of skill in the language domain as the most frequent regression type. However, a meta-analytic review [23] and a study [29] found that either the loss in language skills or in social skills was the most common type of regression, followed by regression in both domains.

The onset age of developmental regression was approximately 2 years (26.24 months for language domain regression and 24.22 months for regression related to other skills). This is consistent with previous studies [10,23], whereas our previous study reported onset age of regression as 31.21 months [5]. Participants in this study were younger than those in our previous study. However, Kim et al. [5] had relatively fewer participants (n=168) than our study (n=1020).

Regarding clinical characteristics, this study revealed significantly higher RRB scores in the group with regression than in the group without. Also, the CARS and SRS total scores indicated that the children with regression had more severe ASD symptoms than those without. Furthermore, lower VABS and IQ scores suggest that children with regression face greater difficulties in adaptive functioning than those without. A recent study [30] observed that more RRBs were associated with delays in overall adaptive skills and lower intellectual abilities. Previous studies have assessed clinical characteristics [5,10]; however, they concluded that regression did not result in significantly different autistic symptom severity. This may be due to the small sample sizes used in these studies (n=168 and n=35, respectively).

In Korea, parents tend to attribute regression in children

to psychological or trauma-related events rather than considering it a phenotype of ASD. It is regarded as a phase that will eventually be recovered from. This phenomenon is mainly because individuals with disabilities have been stigmatized and regarded as a threat to families in Korea. Therefore, they have mistaken ASD for attachment problems, as regression and fixation are symptoms commonly seen in attachment problems. Attachment disorders are typically overcome when the attachment is recovered; therefore, parents tend to regard regression as reversible. However, as we observed in our analysis, only a few children regain the lost skills. Previous studies have emphasized that regression in children with ASD should be regarded with care.

To our knowledge, this is the first study that explored the association between regression and perinatal factors. While significant associations were observed between regression and placenta previa/hypertension, the results should be interpreted cautiously as information on perinatal factors was only available for a subset of the participants (n=669, 65.59%). Further studies need to elucidate the association between the perinatal factors and regression in patients with ASD.

The strengths of this study include the use of a large sample size and of standardized tests to explore regression characteristics. However, this study also had few limitations. First, the developmental information on regression was based on acquired information from retrospective recalls and could be influenced by recall bias. Second, our sample was not age-matched. However, with a comparatively large sample size that only includes children aged 2–7 years, we expect the confounding effect of age to be minimal. Third, perinatal information was acquired for only a subgroup of participants, and thus restricted further analysis.

CONCLUSION

Children with regression and ASD had more severe autistic symptoms, including in behavioral and psychological functioning, suggesting that this group may be a distinct ASD subtype. Therefore, our findings emphasize the importance of keen observation and surveillance regarding developmental regression. Furthermore, interventions targeting children with developmental regression should be considered.

Availability of Data and Material

The datasets generated or analyzed during the study are not publicly available as the IRB approved the data to be used within the research team but could be available from the corresponding author on reasonable request.

Conflicts of Interest

Hee Jeong Yoo, a contributing editor of the *Journal of the Korean Academy of Child and Adolescent Psychiatry*, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Hee Jeong Yoo. Data curation: Ye Rim Kim, Da-Yea Song, Guiyoung Bong. Formal analysis: Ye Rim Kim, Da-Yea Song. Funding acquisition: Hee Jeong Yoo. Investigation: Ye Rim Kim, Da-Yea Song. Methodology: Ye Rim Kim, Da-Yea Song. Project administration: Ye Rim Kim, Da-Yea Song, Guiyoung Bong. Supervision: Hee Jeong Yoo. Writing—original draft: Ye Rim Kim, Da-Yea Song. Writing—review & editing: Guiyoung Bong, Jae Hyun Han, Hee Jeong Yoo.

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