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ORIGINAL ARTICLE

Motor disturbances in children with autism spectrum disorder

Alteraciones motoras en pacientes pediátricos con trastorno del espectro autista

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What do we know about the subject matter of this study?

A high proportion of children with Autism Spectrum Disorder present motor alterations early in life. An association between these disturbances and abnormalities in the development of language and communication skills during childhood has been described.

What does this study contribute to what is already known?

This study reports that in patients with Autism Spectrum Disorder, infant hypotonia is associated with the development of motor impairments throughout childhood, and that walking delay is associated with a lower level of verbal expressive language development in preschoolers.

Abstract

Objective: To describe main motor disorders detected in children with autism spectrum disorder (ASD) and analyze associated clinical variables. **Patients and Method:** A cross-sectional observational study of 96 children with ASD, median age 4 years (range, 3-9), 32.3% girls, and 18.8% preterm. Children were evaluated at the UC-CHRISTUS Clinical Hospital Neurodevelopmental Unit for three years. We analyzed the relationship between motor signs (stereotypies, delayed gait, and hypo/hypertonia) and spoken language at 4 years of age. **Results:** 63.5% of children presented a motor disorder, 33.3% had hand or body motor stereotypies at the time of the evaluation, and 28.1% had delayed gait (> 16 months of corrected gestational age). These children had a higher frequency of absence of spoken language at four years of age (OR = 9.36; 95% CI = 2.67-32.78) than patients without delayed gait. 40.6% of children presented alterations in muscle tone during the first two years of life (32.3% generalized hypotonia and 8.3% generalized hypertonia). A history of generalized hypotonia increases the chance of presenting delayed gait (OR = 2.65; 95% CI = 1.08-6.48) and motor stereotypies (OR = 2.63; 95% CI = 1.04-6.65). **Conclusions:** Children with ASD usually develop motor disorders that may precede the diagnosis of the condition. In ASD, infant hypotonia may predict the occurrence of other motor disorders, and delayed gait was associated with spoken language absence in preschool age.

Keywords:
Autism Spectrum Disorder;
Motor Disturbances;
Hypotonia;
Neurodevelopment

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Introduction

Autism Spectrum Disorder (ASD) encompasses a wide range of qualitative neurodevelopmental disorders with great inter- and intra-individual variability, which are clear from initial stages and persist throughout life. Diagnosis is based on the presence of numerous symptoms and signs organized into two cardinal dimensions. The first one is the presence of impairments in communication and social interaction and the second one is the development of restrictive, repetitive, and unusual behavioral patterns in language, cognitive and motor function, or sensory regulation[1].

Although most affected children show clinical features suggestive of ASD between 18 and 24 months of life, less than 50% are diagnosed before the age of 4[2]. Evidence shows that the long-term functional prognosis of patients with ASD is related to early intervention[3,4]. Therefore, the American Academy of Pediatrics (AAP) suggests universal screening of all children between 18 and 24 months, using standardized and validated instruments for the target population[5,6].

Despite not being among the cardinal symptoms of ASD, many patients present with motor impairment early, usually before meeting the diagnostic criteria for the condition. Furthermore, data from previous studies suggest that it is possible to detect earlier at-risk groups based on motor developmental history and neurological physical examination[7-9].

The goal of this research is to explore the frequency and type of motor disorders present in a series of pediatric patients with ASD, in addition to analyzing the clinical variables associated with these alterations.

Patients and Method

Participants

We included all patients aged 3 to 10 years seen at the Neurodevelopmental Unit of the UC-CHRISTUS Health Network between 2018 and 2020, with a diagnosis of ASD according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM 5)[10] and scoring above the diagnostic cut-off point in Modules 1, 2, and 3 of the Autism Diagnostic Observation Schedule, second edition (ADOS-2)[11].

Patients with cerebral palsy, neuromuscular diseases, inborn errors of metabolism, known chromosome disease or gene mutation, and with incomplete information about history of the age at the onset of gait, alterations of muscle tone within the first 24 months of life, and presence of motor stereotypies were excluded.

The study was approved by the Scientific Ethical Committee of the Faculty of Medicine (CEC-MedUC) of the Pontifical Catholic University of Chile (No. 200918001).

Data collection and variables studied

The electronic medical record of each patient was reviewed and information regarding the diagnosis of ASD and motor disorders was obtained retrospectively. The following variables were recorded in a database: sex, age at the time of the study, age at independent walking (gestational age corrected in months), prematurity (< 37 weeks gestational age), verbal expressive language at 4 years of age (at least 4 words with communicative meaning, between 48 and 59 months of life), alterations in muscle tone during the first 24 months of life (decreased or increased muscle tone of the 4 limbs and trunk, defined by a pediatric neurologist), and motor stereotypies (repetitive and purposeless manual or body movements that occur in a specific pattern)[12].

Statistical analysis

Categorical variables were expressed as absolute and relative frequencies, while continuous variables were expressed as median and interquartile range (IQR). Bivariate analysis was performed to determine the presence, direction, and magnitude of possible associations between the different motor disorders studied and other clinical characteristics by calculating Odds Ratios (ORs) with their respective 95% confidence intervals (95% CI). Data analysis was performed using the Stata/IC 16.1 statistical package. A $p < 0.05$ value was considered statistically significant.

Results

Sample characteristics

Of 102 pediatric patients with ASD who met the study criteria, 6 were excluded due to incomplete data. Among the 96 children included in the final analysis, the median age at the time of the study was 4 years (IQR, 3-5), the sex distribution was 65 males (67.7%) and 31 females (32.3%), 18 patients (18.8%) were preterm newborns, and 22 (22.9%) have some associated comorbidity (Table 1). Among the 66 children aged 4 years at the time of the study, 17 (25.8%) had no verbal language.

Frequency of motor disorders

Sixty-one children (63.5%) were detected with some of the motor disorders studied, including abnormalities in muscle tone during the first 2 years of life (39 patients, 40.6%), motor stereotypies (32 patients, 33.3%), and delayed walking (27 patients, 28.1%). Among the alterations of muscle tone, 31 children

(32.3%) had hypotonia and 8 patients (8.3%) had generalized hypertonia. We detected 8 patients (8.3%) with fluctuating generalized hypertonia and abnormal postures. We did not observe spasticity in the patients evaluated.

Delayed independent walking

The median age at the onset of independent walking was 14 months (IQR, 12-17). When analyzing the relationship between gait delay (independent walking after 16 months of corrected gestational age) and the absence of verbal language at 4 years of age, there was a positive association between both variables in this group of patients (Table 2).

Association between motor disorders

Children with generalized muscle hypotonia within the first 2 years of life were more likely to have gait delay (OR = 2.65; 95% CI = 1.08-6.48) and motor stereotypies (OR = 2.63; 95% CI = 1.04-6.65). No significant association was seen between gait delay and the presence of motor stereotypies (p = 0.152).

Discussion

This study evaluated the frequency of motor disorders in a series of patients with a diagnosis of ASD aged 3 to 10 years. About two-thirds of the children evaluated had history of muscle tone impairment during the first 2 years of life, delayed acquisition of independent walking, or motor stereotypies at the time of evaluation.

The high frequency of generalized hypotonia in our patients -over one-third of the children evaluated- is in line with the findings of earlier observational studies that have shown that this alteration of muscle tone is present in 15 to 67% of individuals with ASD during the first 5 years of life[13-16]. Additionally, our results showed that a history of infant hypotonia is associated with an increased likelihood of presenting with other motor disorders in this group of patients, supporting the hypothesis of a possible etiological relationship between the different motor functioning alterations present in children with ASD[9,15,17,18]. Although alterations in muscle tone during the first years of life are syndromes with multiple etiologies, in the context of infants presenting with alterations in joint attention, this finding could predict motor abnormalities and future autistic symptomatology[19].

Almost one-third of the patients evaluated in our study have a history of delay in the acquisition of independent walking, a figure considerably higher than the 3% reported by the World Health Organization (WHO) for the general pediatric population[20]. These results are in line with the findings of previous studies that have shown a higher prevalence of motor developmental delay in children with ASD when compared with typically developing children and children with other neurodevelopmental disorders[15,21].

In a study conducted by the Autism Center at the New Jersey Medical School-University of Medicine and Dentistry, which analyzed data from 154 children with ASD, it was seen that the prevalence of motor developmental delay in these patients was 9%, independent of the severity of autistic symptomatology[15].

A recent study conducted by the University Children's Hospital Basel in Switzerland, compared data from 32 patients with non-syndromic ASD (ages 4 to 16 years) with level 2 to 3 of symptoms severity[10], with data from 36 typically developing controls (ages 4 to 16) from the same base population, and concluded that children with ASD walked independently at a significantly older age than controls (16.4 months (SD 6.23) versus 13.3 months (SD 1.23), p 0.012) and also had a greater degree of qualitative gait disturbances during the second year of life (increased base of support and balance disturbances, p < 0.001) than controls[18].

Our data show that children with autism and gait delay are more likely to lack verbal expressive language at 4 years of age, supporting the direct relationship between gross motor and language delay in children with ASD, including in clinical practice, cases of global developmental delay that are later categorized as ASD

Table 1. Baseline characteristics of studied children

Characteristics	n (%)
Sex	
Male	65 (67.7)
Female	31 (32.3)
Age	
3 to 4 years	30 (31.3)
5 to 10 years	66 (68.8)
Preterm newborn	18 (18.8)
Absence of expressive verbal language at 4 years*	17 (25.8)
Comorbidity	22 (22.9)
Febrile seizures	5 (5.2)
CNS infections, TBI, and HIE	13 (13.5)
Epilepsy	7 (7.3)
Motor disorders	61 (63.5)
Infant muscle tone abnormalities	39 (40.6)
Generalized hypotonia	31 (32.3)
Generalized hypertonia	8 (8.3)
Walking delay	27 (28.1)
Motor stereotypies	32 (33.3)

Abbreviations. CNS: central nervous system; TBI: traumatic brain injury; HIE: neonatal hypoxic-ischemic encephalopathy. *Among 66 patients aged ≥ 4 years at analyses.

Table 2. Bivariate analysis of the relationship between motor disorders and other clinical features (n = 93)

	OR	95% CI
Any motor disorder		
Male sex	1.73	(0.72-4.15)
Preterm newborn	1.63	(0.53-5.02)
Comorbidity†	1.01	(0.37-2.70)
Not-verbal at 4 years*	3.50	(0.89-13.8)
Generalized hypotonia		
Male sex	2.60	(0.94-7.23)
Preterm newborn	0.21	(0.05-0.99)
Comorbidity†	0.54	(0.18-1.64)
Not-verbal at 4 years*	0.70	(0.20-2.50)
Motor stereotypies	2.65	(1.08-6.48)
Walking delay	2.63	(1.04-6.65)
Motor stereotypies		
Male sex	1.68	(0.65-4.35)
Preterm newborn	1.00	(0.34-2.97)
Comorbidity†	1.54	(0.58-4.10)
Not-verbal at 4 years*	0.70	(0.20-2.50)
Walking delay	1.96	(0.78-4.92)
Walking delay		
Male sex	1.19	(0.45-3.12)
Preterm newborn	0.45	(0.12-1.70)
Comorbidity†	0.70	(0.23-2.12)
Not-verbal at 4 years*	9.36	(2.67-32.8)

†Central nervous system infections, traumatic brain injury, neonatal hypoxic-ischemic encephalopathy. *Among 66 patients aged ≥ 4 years at analyses.

at preschool age. In this regard, an analytical cross-sectional study conducted at the UC Davis MIND Institute analyzed data from 103 pediatric patients (54 with a diagnosis of ASD, 24 with typical development, and 25 with developmental delay without autistic symptoms) from 2 referral centers in the United States, and concluded that patients with typical development presented average independent walking at a significantly younger age than children with ASD and language regression (10.9 months (SD 0.36) versus 13.4 months (SD 0.57), $p < 0.01$). However, there was no significant difference in the age at the onset of average independent walking between children with typical development and ASD without language regression (12.17, SD 0.46, p 0.1), suggesting that motor functioning might modulate language development in children with ASD[16].

Finally, although the presence of abnormal movements, especially motor stereotypies, suggests the diagnostic possibility of ASD, they are also often found in typically developing children and adults and in individuals presenting with isolated sensory dysregulation, developmental language disorders, or intellectual disability[22,23]. Although there is great heterogeneity in the definition of stereotypies, a 2016 systematic review showed that the overall prevalence of stereotypies in developmental disorders is around 52%[24], figures slightly higher than those found in this study.

Data collection in a center specialized in the diagnosis and treatment of neurodevelopmental disorders limits the extrapolation of the results of this study to the general population. In addition, only a circumscribed number of motor disorders were included in the analysis, excluding other alterations that could have clinical relevance. However, the main strengths of the study are the relatively low proportion of patients excluded due to incomplete data (5.9%), the collection and recording of data in a pre-designed record close to the time of occurrence of each clinical variable studied, and the diagnosis of ASD made according to DSM 5 criteria, defining autistic symptomatology with the main diagnostic tool available (ADOS-2).

The findings of this study suggest that most patients with ASD present motor disorders during the first years of life, which may precede the definitive diagnosis of the condition. The higher frequency of absence of verbal language at age 4 years in children with gait delay is evidence of the potential role of the motor system in the development of ASD.

Due to their special clinical characteristics, prospective studies are needed to evaluate the functional prognosis and quality of life of children with ASD who present quantitative and qualitative alterations in motor development.

Conclusions

The presence of neurological symptoms and signs during the infancy period would allow the identification of groups at risk for the development of ASD during childhood, so it is suggested that, in addition to the screening tools applied in primary care during the second year of life (included in the AAP recommendations), infants with motor developmental disorders should be evaluated early by multidisciplinary teams with training in neurodevelopmental disorders.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: This study was approved by the respective Research Ethics Committee, which, according to the study's characteristics, has accepted the non-use of Informed Consent.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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