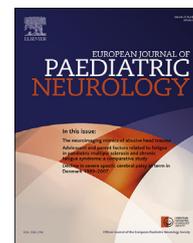




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## Original article

# Gait in children with infantile/atypical autism: Age-dependent decrease in gait variability and associations with motor skills



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## ABSTRACT

Gait and its associations with prewalking motor milestones, motor skills, and age were investigated in 32 children with infantile/atypical autism and 36 typically developing controls. Gait was assessed using GAITRite recordings of spatiotemporal and variability gait parameters. Parents reported their child's prewalking motor milestones. Motor skills were assessed using the Movement Assessment Battery for Children. Children with infantile/atypical autism showed higher gait variability than controls, indicating a less regular walking pattern. In children with infantile/atypical autism gait variability was negatively associated with motor skills, but there was no such association with prewalking motor milestones. The higher gait variability in children with infantile/atypical autism showed an age-dependent decrease, suggesting that their gait regularity converges toward that of typically developing children.

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Autism spectrum disorder (ASD) is an inclusive term for a group of biologically based neurodevelopmental disorders characterized by the core symptoms of impairments of social communication and repetitive behaviors with limited interests.<sup>1</sup> Furthermore, it has been suggested that motor dysfunction may also be a core symptom of ASD and may predate social and communicative impairments.<sup>2,3</sup>

Motor symptoms of children with ASD involve delays in motor milestone development, with findings indicating that

children with ASD acquire abilities such as sitting and walking autonomously several months later than typically developing children,<sup>4,5</sup> who reach these motor milestones approximately at the age of 6 and 12 months, respectively.<sup>6</sup> Further, children with ASD show impairments in motor skills, including difficulties with gross and fine motor function and coordination.<sup>7–13</sup> Impaired motor development in individuals with ASD can compromise the ability to perform activities of daily living (e. g. tying shoes, writing, as well as social play such as

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riding a bike, throwing a ball, and participating in team sports).<sup>12</sup>

Gross motor impairments can lead to clumsy movement patterns—including walking, which is the most important mode of human locomotion.<sup>14,15</sup> In this vein, Shetreat-Klein<sup>16</sup> reported the qualitative finding that during walking, children with ASD lack consistency, smoothness, and coordination compared to controls. Furthermore, it has been observed that children with ASD are more prone to idiopathic toe walking than typically developing children.<sup>17–19</sup>

However, so far, only a small number of empirical studies have investigated walking patterns of children with ASD using quantitative methods, such as electronic walkway systems or electronic footswitches. Early research in children with ASD focused on alterations in spatiotemporal gait measures such as reduced stride length and increased stride time with inconsistent results.<sup>20–27</sup>

In contrast to the inconsistency in findings on spatiotemporal gait parameters, a more homogeneous picture emerges for measures of gait variability (i.e., stride-to-stride fluctuations), representing the regularity and automaticity of gait.<sup>28</sup> Studies assessing gait variability have consistently reported higher gait variability among children with ASD compared to typically developing children.<sup>26,27,29</sup> For example, Nayate<sup>29</sup> investigated 11 children (average age: 12.8 years) diagnosed with ASD, who showed significantly increased variability for stride length as well as increased step width compared to controls. This is in line with the findings reported by Rinehart<sup>26</sup> of increased stride length variability in a sample of 10 children with ASD (average age: 10.7 years) compared to typically developing controls but without further dissimilarities for spatiotemporal measures such as velocity and stride length between the two groups. The same holds true for the findings reported by Rinehart<sup>27</sup> of no between-group differences for spatiotemporal measures (e.g., velocity, stride length), whereas stride length variability and stride time variability were significantly increased in their sample of 11 children with ASD (average age: 5.8 years) compared to controls. These findings may lend further support to the notion that measures of gait variability provide a more discriminant and sensitive measure of gait performance than spatiotemporal gait variables.<sup>28,30</sup>

In terms of gait development, previous results on walking performance of typically developing children have shown that spatiotemporal and variability measures of gait appear to develop in a particular direction for a certain period of time. Children of older age show improved spatiotemporal gait measures, among those velocity and step length and present with a mature gait pattern by the age of seven years.<sup>14,31,32</sup> Gait variability, on the other hand, further develops beyond this age with gait becoming more regular during middle and late childhood before reaching maturity in adolescence.<sup>31,33–36</sup> These findings illustrate the relevance of taking not only spatiotemporal measures into consideration, but also variability measures when it comes to gait analysis. Although percentage limited portion of children with ASD lose their symptoms that support a diagnosis of ASD at some point during their life,<sup>37</sup> findings on outcomes during adolescence and adulthood suggest that in most cases ASD is a lifelong condition that involves persistent and stable impairments in

mental, linguistic, social, and motor abilities.<sup>38–40</sup> So far, it has not been investigated whether this also holds true for gait impairments of children with ASD. Nonetheless, studies of children with other neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD) have indicated that their initially higher gait variability shows an age-dependent decrease, with gait performance becoming more regular and converging toward typically developing controls during childhood.<sup>41</sup> However, for subjects with ASD it is still uncertain whether this developmental pattern also emerges or whether the previously reported alterations of gait variability<sup>26,27,29</sup> remain persistent and therefore nonconvergent toward controls during childhood.

In sum, several studies reported impaired motor development in children with ASD, including delayed acquisition of early motor milestones (e.g., sitting and walking autonomously<sup>4,5</sup>), impaired motor function involving fine and gross motor skills,<sup>12</sup> and alterations in spatiotemporal and variability gait characteristics. And yet, there is still significant data missing from the research: Although signs of impaired motor development possibly affecting later gait development may be present as early as infancy in subjects with ASD,<sup>3</sup> no study has so far investigated whether prewalking motor milestones such as sitting and walking autonomously are associated with later gait development. Furthermore, whereas recent studies indicated impairments of motor skills<sup>13</sup> and higher gait variability<sup>29</sup> in children with ASD, no study has investigated possible associations between motor skills and gait variability. Additionally, it remains unclear whether in children with ASD gait variability measures show age-dependent alterations during childhood. The aim of the present study was therefore to further examine gait performance and to collect information on prewalking motor milestones as well as to assess motor skills of children with ASD by including a larger sample with a wider age range than used in previous studies. We hypothesized that children with ASD would show a less stable and less regular walking pattern than controls. Additionally, we hypothesized that children with ASD would show a delayed acquisition of motor milestones and impairments in motor skills. Finally, to address what has been lacking in research, we explored whether measures of gait variability are associated with motor milestones and motor skills. Further we studied whether — with increasing age — gait variability measures of children with ASD decrease or remain persistent and nonconvergent toward that of typically developing children.

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## 1. Methods

### 1.1. Participants

Our group of patients were picked from an original cohort of 98 patients who were diagnosed with ASD according to the ICD-10<sup>42</sup> and were treated between 2008 and 2013 at the University Children's Hospital Basel (Switzerland). Given that previous studies indicated differences between children with Asperger's syndrome (AS) and children with infantile or atypical autism in their neurological basis, clinical characteristics, and comorbidities<sup>43</sup> as well as differences in motor

performance<sup>44</sup> including gait patterns,<sup>26</sup> we excluded children with AS or pervasive developmental disorder not otherwise specified (PDD-NOS) from the present study. Furthermore, children with comorbid cerebral palsy or otherwise-classified motor handicap were excluded from the recruitment process. Of the remaining 52 children, six children were unreachable, and 38 of the 46 who could be contacted by phone consented to taking part in the study. For 2 children data collection was not possible because they did not understand the test instructions or were noncompliant. Four children with ASD showed idiopathic toe walking resulting in erroneous gait data and consequently had to be excluded from data analysis.

In the end, the study group contained 32 children aged between 4.1 and 16.9 years (mean age = 9.2 years; 27 boys, 5 girls) including 29 children diagnosed with infantile autism and three children with atypical autism independent of a genetic aetiology. A genetic examination was performed in 10 of the 32 children diagnosed with infantile or atypical autism with karyotype, exclusion of fragile X syndrome, or exclusion of other microdeletion syndromes using microarray-based comparative genomic hybridization. For two of those children a genetic disorder was confirmed (Klinefelter syndrome, deletion Xp22.11). 1 child is under medication because of epilepsy, one is medicated because of inattention (see Table 1).

For the control group from private surroundings of co-workers were recruited. The control group consisted of 36 children aged between 4.1 and 16.5 years (mean age = 9.0 years, 31 boys, 5 girls). Table 1 summarizes group characteristics as well as medication status of children with infantile/atypical autism. As shown in Table 1, the two groups of children were similar with respect to age, sex, height, weight, and leg length.

## 2. Materials

### 2.1. Gait assessment

Gait was measured using the GAITRite electronic walkway system (GAITRite Platinum; CIR Systems, USA). This system consists of a 701-cm-long walkway with 23,040 integrated pressure sensors. A 1.25-m nonrecordable zone was added on each end of the walkway to minimize the effects of acceleration

and deceleration. Therefore, children walked approximately 10 m per walk and each walk comprised on average eight steps. The use of GAITRite for children when assessing gait is well established.<sup>45</sup> All gait analyses were performed according to the European guidelines for spatiotemporal gait analysis.<sup>46</sup> The following seven spatiotemporal and variability measures of gait were evaluated: velocity (obtained by dividing the distance traveled by ambulation time expressed in centimeters per second); stride time (the time elapsed between the first contact of two consecutive footfalls of the same foot expressed in seconds); stride length (the distance between the heel points of two consecutive footfalls of the same foot expressed in centimeters); base of support (the perpendicular distance from heel point of one footfall to the line of progression of the opposite foot expressed in centimeters); gait variability, assessed as variability in stride velocity, stride time, and stride length using the percentage coefficient of variation (CV = standard deviation/mean × 100). When assessing gait outcome, velocity is the most often used general indicator of functional performance,<sup>47</sup> while other variables such as stride length and stride time reflect gait patterning,<sup>48</sup> and base of support measures equilibrium.<sup>29</sup> Gaitvariability, on the other hand, reflects the regularity of gait and forms a more discriminant and sensitive measure of subtle changes in gait performance.<sup>28</sup> Height, weight, and leg length were measured prior to gait assessment. The patients received one demonstration and a practice walk before then performing a total of ten trials of walking at their normal pace. Each walk was individually analyzed using GAITRite software. For further data analysis, the gait parameter were then averaged over the ten walking trials.

### 2.2. Motor milestones and motor skills assessment

Information about motor milestones was gathered by asking the parents to report at what age (in months) their child was able to sit upright autonomously and walk autonomously. Motor skills were assessed using the German version of the Movement Assessment Battery for Children, 2nd edition (M-ABC-2),<sup>49</sup> which is an individually administered standardized measure of motor function for children from 3 to 16 years of age with established reliability and validity.<sup>50</sup> There are three age-related item sets, each consisting of eight tasks measuring manual dexterity (three tasks), ball skills (two tasks), and balance (three tasks). Item scores can be combined to form an overall score with a normative mean of 10 and standard deviation of 3.

### 2.3. Statistical analysis

Data were analyzed using IBM SPSS Statistics (Version 20). To test for group differences in demographic characteristics, a  $\chi^2$  test for categorical variables or an independent samples t test for continuous variables was used. Group differences in spatiotemporal and variability measures of gait, as well as motor milestones and motor skills, were assessed using multivariate analysis of variance (MANOVA). The F statistic, p value (two tailed), and effect sizes ( $\eta^2$ ) are reported. If an extreme value (defined as a score exceeding 3 SDs from the group mean) occurred in the gait measures, scores were truncated to  $\pm 3$  SD.

**Table 1 – Demographic characteristics of children with infantile/atypical autism and controls.**

Characteristic	ASD (n = 32) <sup>a</sup>	Controls (n = 36)	p
Age (years)	9.2 (3.8)	9.0 (3.8)	.81
Sex (girls:boys)	5:27	5:31	.84
Height (cm)	131.4 (41.2)	136.4 (22.0)	.52
Weight (kg)	39.7 (21.9)	33.4 (16.5)	.19
Leg length (cm) <sup>b</sup>	74.1 (16.2)	72.7 (14.6)	.71

Note. Data are mean (SD) or number; p values are given for independent t test or  $\chi^2$  test.

<sup>a</sup> Nine patients (Ps) were medicated: P1, sultiame and levetiracetam; P2, P3, melatonin; P4–P7, risperidone; P8, risperidone and melatonin; P9, methylphenidate.

<sup>b</sup> Leg length was measured with footwear from greater trochanter to the floor, bisecting the lateral malleolus.

Further, we assessed whether gait variability was connected to motor milestones and motor skills, and if so, whether children with infantile/atypical autism presented differently to typically developing children in these areas. As we were interested in a general marker of motor skills, the M-ABC-2 overall score was included in the following analyses. To analyze whether associations of gait variability with motor milestones and motor skills differed in children with infantile/atypical autism and controls (i.e., whether group [infantile/atypical autism vs. control] acted as a moderator of these associations), three hierarchical regression analyses were conducted following the procedure proposed by Aiken.<sup>51</sup> In each hierarchical regression the control variable leg length was entered in the first block. Then, group (infantile/atypical autism vs. control) and the respective predictor (i.e., sit upright autonomously, walk autonomously, or M-ABC-2 overall score) were entered in the next block. Finally, the interaction term between group (infantile/atypical autism vs. control) and the corresponding predictor was entered in the last block.

Additionally, a hierarchical regression was conducted to examine whether the association between gait variability measures and age differed in children with infantile/atypical autism and controls (i.e., whether group [infantile/atypical autism vs. control] acted as a moderator of the association). The control variable leg length was entered in the first block. Group (infantile/atypical autism vs. control) and age were entered in the next block and in the last block the interaction term Group (infantile/atypical autism vs. control)  $\times$  Age was entered.

If a significant interaction was found (indicating a significant moderation effect), then the interaction was graphed by computing the predicted gait variability measures separately for children with infantile/atypical autism and controls. Single slope analyses were used to evaluate whether the slopes in the graphs were significantly different from zero.<sup>51</sup> (Aiken et al., 1991).

### 3. Results

#### 3.1. Gait measures, motor milestones, and motor skills of children with infantile/atypical autism and controls

The results of the gait measures, motor milestones, and motor skills are presented in Table 2. For gait measures, the MANOVA revealed a significant effect of group (Wilks's multivariate test),  $F(7,60) = 8.709$ ,  $p < .001$ ,  $\eta^2 = .504$ , with univariate tests showing significant higher values for children with infantile/atypical autism on all measures of gait variability: CV stride velocity ( $p = .001$ ,  $\eta^2 = .167$ ); CV stride time ( $p < .001$ ,  $\eta^2 = .207$ ); and CV stride length ( $p < .001$ ,  $\eta^2 = .174$ ), as well as base of support ( $p < .001$ ,  $\eta^2 = .196$ ), whereas no group differences emerged for the other spatiotemporal gait measures velocity, stride time, and stride length.

For motor milestones the MANOVA revealed a significant effect of group (Wilks's multivariate test),  $F(2,53) = 4.406$ ,  $p = .017$ ,  $\eta^2 = .143$ , with univariate tests showing that children with ASD were able to sit upright autonomously at a similar age as controls at approximately 7–8 months, but that controls were able to walk autonomously at about 13.3

months and thus at an earlier age than children with infantile/atypical autism who walked at about 16.4 months ( $p = .012$ ,  $\eta^2 = .111$ ).

Furthermore, for motor skills assessed with the M-ABC-2, the MANOVA revealed a significant effect of group (Wilks' multivariate test),  $F(4,50) = 21.991$ ,  $p < .001$ ,  $\eta^2 = .638$ , with univariate tests showing significant lower scores of children with ASD on all three subscales of the M-ABC-2—manual dexterity ( $p < .001$ ,  $\eta^2 = .419$ ); ball skills ( $p < .001$ ,  $\eta^2 = .363$ ); and balance ( $p < .001$ ,  $\eta^2 = .487$ ) — as well as for the M-ABC-2 overall score ( $p < .001$ ,  $\eta^2 = .597$ ; Table 2).

#### 3.2. Associations of gait variability measures with motor milestones and motor skills

Controlled for leg length, motor milestones (i.e., sit upright autonomously, walk autonomously) showed no significant associations with gait variability in a hierarchical regression analysis, whereas a higher M-ABC-2 overall score was significantly associated with lower scores on all gait variability measures: CV stride velocity ( $\beta = -.423$ ,  $p = .016$ ), CV stride time ( $\beta = -.350$ ,  $p = .045$ ), CV stride length ( $\beta = -.375$ ,  $p = .027$ ).

Next moderated hierarchical regression analyses were calculated with interaction terms between group (infantile/atypical autism vs. control) and the predictors (i.e., sit upright autonomously, walk autonomously, M-ABC-2 overall score), controlling for leg length and the corresponding predictor. These analyses revealed three significant interaction terms (Table 3): Group (infantile/atypical autism vs. control) moderated the association between M-ABC-2 overall score and CV stride velocity ( $\beta = .310$ ,  $p = .015$ ), CV stride time ( $\beta = .315$ ,  $p = .014$ ), and CV stride length ( $\beta = .254$ ,  $p = .042$ ).

As depicted in Fig. 1, in children with ASD, the M-ABC-2 overall score was significantly associated with all measures of gait variability: CV stride velocity ( $\beta = -.591$ ,  $p = .010$ ), CV stride time ( $\beta = -.567$ ,  $p = .013$ ), and CV stride length ( $\beta = -.531$ ,  $p = .018$ ), such that higher M-ABC-2 overall scores were related to lower gait variability. In controls there were no significant associations between their M-ABC-2 overall score and gait variability measures.

#### 3.3. Associations of gait variability measures with age

Controlling for leg length, hierarchical regression analyses for the combined sample showed that age was significantly associated with lower scores on all gait variability measures: CV stride velocity ( $\beta = -.529$ ,  $p = .004$ ), CV stride time ( $\beta = -.566$ ,  $p = .002$ ), CV stride length ( $\beta = -.541$ ,  $p = .002$ ). Further, moderated hierarchical regression analyses were calculated with group (infantile/atypical autism vs. control)  $\times$  Age interaction terms, controlling for leg length and age. These analyses revealed three significant interaction terms (Table 3). Group (infantile/atypical autism vs. control) moderated the association between age and CV stride velocity ( $\beta = .197$ ,  $p = .034$ ), CV stride time ( $\beta = .269$ ,  $p = .002$ ), and CV stride length ( $\beta = .207$ ,  $p = .017$ ).

As depicted in Fig. 2, in children with infantile/atypical autism, age was significantly associated with all measures of gait variability: CV stride velocity ( $\beta = -.802$ ,  $p = .004$ ), CV

**Table 2 – Statistical results from the MANOVAs comparing gait measures (spatiotemporal and variability measures), motor milestones, and general motor skills of children with infantile/atypical autism and controls.**

Measures	Infantile/atypical autism	95% CI	Controls	95% CI	F	p	$\eta^2$
<i>Gait measures</i>							
Velocity (cm/s)	126.95 (31.19)	[118.15, 135.44]	124.15 (17.58)	[115.86, 132.44]	0.214	.645	.003
Stride time (s)	0.99 (0.20)	[0.94, 1.06]	0.98 (0.11)	[0.93, 1.04]	0.089	.767	.001
Stride length (cm)	119.71 (20.68)	[112.55, 126.86]	121.25 (19.90)	[114.50, 127.99]	0.098	.755	.001
Base of support (cm)	10.47 (2.40)	[9.64, 11.41]	8.40 (1.85)	[7.71, 9.09]	16.049	<.001	.196
CV stride velocity (%)	6.42 (3.99)	[5.31, 7.52]	3.65 (2.07)	[2.61, 4.69]	13.246	.001	.167
CV stride time (%)	5.05 (3.42)	[4.17, 5.93]	2.54 (1.18)	[1.71, 3.37]	17.259	<.001	.207
CV stride length (%)	4.95 (2.79)	[4.16, 5.74]	2.92 (1.58)	[2.18, 3.66]	13.921	<.001	.174
<i>Motor milestones</i>							
Sit upright autonomously (months)	8.08 (3.96)	[6.72, 8.90]	7.30 (1.31)	[6.30, 8.51]	1.108	.297	.020
Walk autonomously (months)	16.37 (6.23)	[13.71, 17.54]	13.31 (1.23)	[11.64, 15.25]	6.725	.012	.111
<i>General motor skills</i>							
M-ABC-2 overall score <sup>a</sup>	4.76 (2.14)	[3.69, 5.83]	10.89 (2.59)	[10.06, 11.71]	83.227	<.001	.597
Manual dexterity	4.57 (2.80)	[3.34, 5.80]	9.54 (2.81)	[8.59, 10.49]	41.136	<.001	.419
Ball skills	6.19 (2.76)	[4.76, 7.61]	11.09 (3.51)	[9.98, 12.19]	29.590	<.001	.363
Balance	6.81 (2.48)	[5.74, 7.88]	11.74 (2.42)	[10.92, 12.57]	53.582	<.001	.487

Note. Data are mean (SD), 95% confidence interval (95% CI), F statistics, p values, and effect size ( $\eta^2$ ).

<sup>a</sup> Standard score normative mean = 10, standard deviation = 3. CV = Coefficient of variation. M-ABC-2 = Movement Assessment Battery for Children, 2nd edition.

stride time ( $\beta = -.818$ ,  $p = .003$ ), CV stride length ( $\beta = -.800$ ,  $p = .002$ ), such that higher age was related to lower gait variability, whereas in controls there were no associations between age and gait variability measures.

#### 4. Discussion

The aim of our study was to examine gait and its associations with prewalking motor milestones as well as with motor skills in children with infantile/atypical autism. Moreover, we aimed to examine age-dependent alterations of gait performance and tested whether with increasing age, gait variability of children with infantile/atypical autism decreases and converges toward that of typically developing children.

As stated in previous studies,<sup>26,27,29</sup> we found that children with infantile/atypical autism walked with significantly higher gait variability (i.e., higher variability for stride velocity, stride time, and stride length) and a significantly wider base of support than controls. These findings back the theory of a less regular and less steady walking pattern in children with ASD.<sup>16,52</sup> Furthermore, in line with Rinehart,<sup>26,27</sup> we found no group differences for velocity, stride time, or stride length such that children with infantile/atypical autism did not show any significant alterations in these gait parameters compared to controls. Hence, our finding that children with infantile/atypical autism show similar performance in spatiotemporal gait measures compared to typically developing children but appear to show difficulties with the regularity of gait cycles (i.e., higher gait variability) highlights the importance of including variability measures, as they may provide a more discriminant and sensitive measure of gait performance than other gait parameters.<sup>28,30</sup>

Our results reveal that the two groups of children were able to sit upright autonomously at a similar age, between the 7th and 8th month of life. On the other hand, children from the control group were able to walk autonomously at an earlier

age (i.e., mean age 13.3 months) than children with infantile/atypical autism (i.e., mean age 16.4 months). This is in accordance with earlier studies showing that age at initial walking autonomously is delayed in children with ASD<sup>3–5,53</sup> whereas only marginal differences were reported for the age at first sitting autonomously.<sup>53</sup> When examining gross motor development, including sitting and walking autonomously, of infants later diagnosed with ASD, Ozonoff et al.<sup>53</sup> reported a slower rate of development for walking compared to typically developing controls. However, our results indicate that those early motor milestones are not associated with development of gait regularity of children with infantile/atypical autism later in childhood, since we found no significant association of the age of sitting and walking autonomously with any measures of later gait variability. Therefore, our findings provide preliminary evidence to refute the assumption that the age of reaching the motor milestones of sitting and walking autonomously during infancy will predict later gait development during childhood and into adolescence among subjects with infantile/atypical autism. However, it is notable that the information on early motor milestones is based on retrospective parental reports in our study and hence needs to be interpreted with caution.

In line with previous research,<sup>9,10,12,54</sup> our findings additionally show that children with infantile/atypical autism had significant difficulties with motor skills, represented by a lower M-ABC-2 overall score compared to controls and significant impairments in each of the areas examined by this test: manual dexterity, ball skills, and balance. Furthermore, our results are the first to show that motor skills assessed by the M-ABC-2 overall score are associated with gait regularity in children with infantile/atypical autism, such that better motor skills go along with a more regular walking pattern (i.e., lower gait variability measures), whereas no such association was found for controls. Hence, gait regularity can be assumed to be a further dimension of motor dysfunction associated with ASD<sup>13</sup> and may be part of a more general impairment in

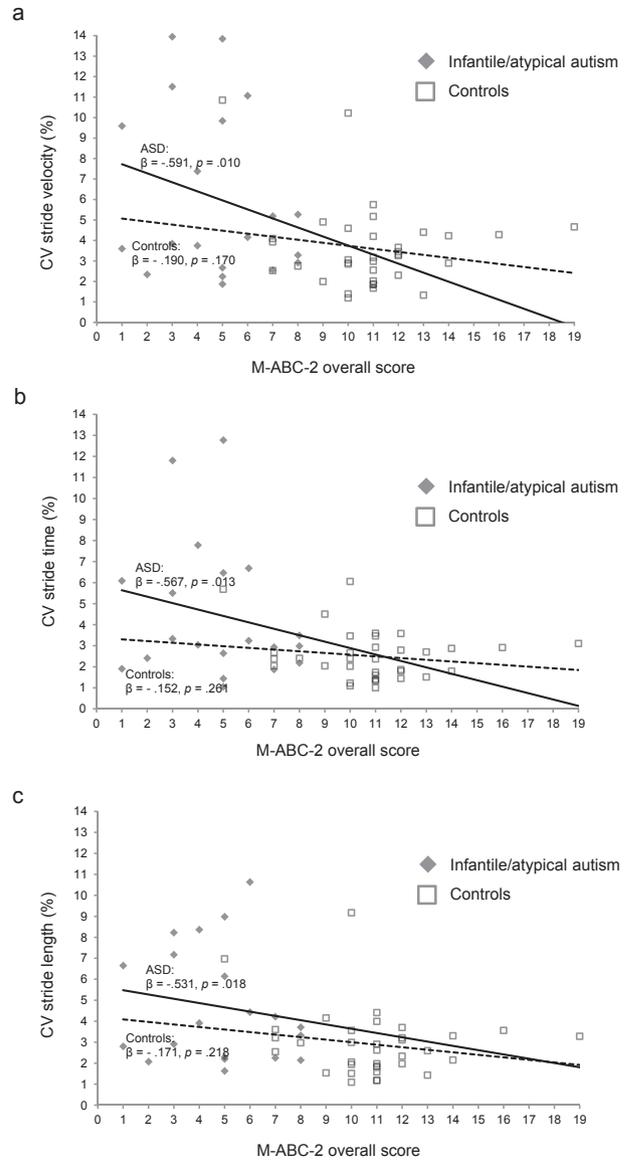
**Table 3 – Hierarchical regressions with Group × Motor milestones (2a, b), Group × Motor skills (2c), and Group × Age (2d) interactions predicting gait variability measures.**

Predictor	CV stride velocity	CV stride time	CV stride length
<b>Step 1</b>			
Leg length	-.396*	-.386*	-.463**
Group (infantile/atypical autism vs. control)	-.462**	-.515**	-.502**
F of total model	.10.067*	9.462*	14.732**
<b>Step 2a</b>			
Sit upright autonomously	-.034	-.057	-.085
Group (infantile/atypical autism vs. control) × sit upright autonomously	.125	.113	.095
F change of interaction	.569	.501	.390
F of total model	7.616**	9.061**	11.122**
<b>Step 2b</b>			
Walk autonomously	-.135	-.038	-.058
Group (infantile/atypical autism vs. control) × walk autonomously	-.131	-.093	-.289
F change of interaction	.266	.141	1.471
F of total model	8.092**	9.354**	11.132**
<b>Step 2c</b>			
M-ABC-2 overall score	-.423*	-.350*	-.375*
Group (infantile/atypical autism vs. control) × M-ABC-2 overall score	.310*	.315*	.254*
F change of interaction	6.322*	6.428*	4.336*
F of total model	12.065**	11.604**	12.608**
<b>Step 2d</b>			
Age	-.529*	-.566*	-.541*
Group (infantile/atypical autism vs. control) × age	.197*	.269**	.207*
F change of interaction	4.715*	10.086**	6.011*
F of total model	14.620**	19.269**	19.512**

Coefficients are standardized regression coefficients unless otherwise indicated. Sex: -1 = boy; +1 = girl. Group: -1 = infantile/atypical autism; +1 = control. M-ABC-2 = Movement Assessment Battery for Children, 2nd edition. CV = Coefficient of variation. \* $p \leq .05$ ; \*\* $p \leq .001$ .

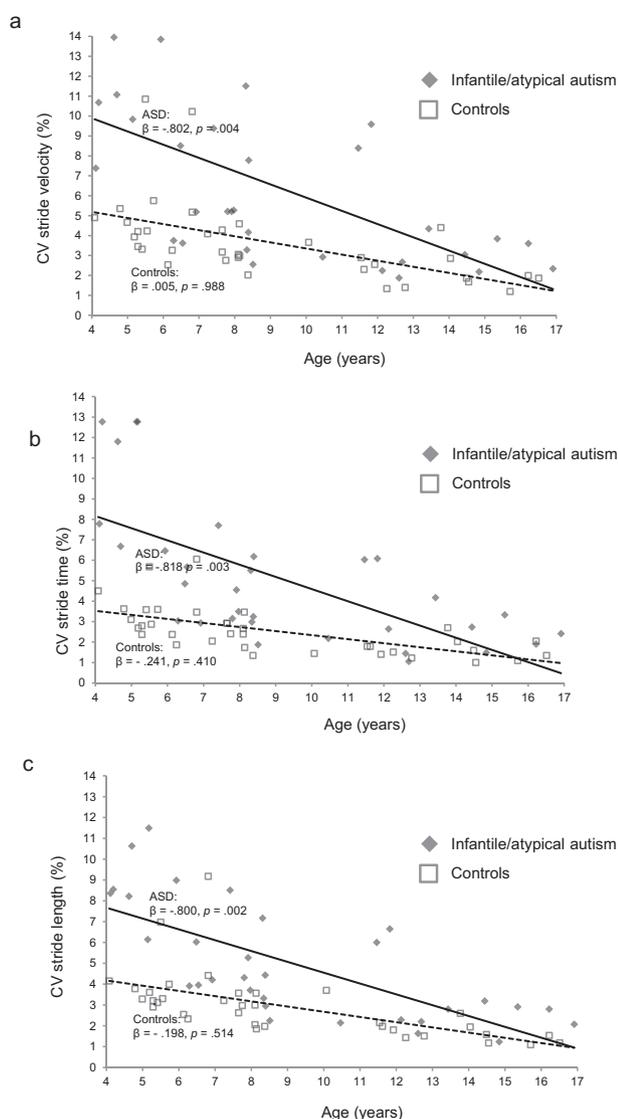
movement that ranges from fine and gross motor skills measured by the M-ABC-2 to the planning and execution of skilled motor sequences such as walking.<sup>55</sup>

Additionally, we discovered that age was connected to all gait variability measures in that with increasing age, variability in stride velocity, stride length, and stride time decreased. These findings confirm the idea that gait evolves continuously during childhood and becomes more regular toward adolescence.<sup>31,33–36</sup> Additionally, we found that children with infantile/atypical autism displayed an age-dependent decrease of their gait variability toward that of controls. A similar developmental pattern has recently been reported in a sample of children with ADHD aged 8–13 years (off or without medication) with gait performance becoming more regular with increasing age and converging toward that of typically developing controls.<sup>41</sup> Although ASD and ADHD are each distinguished by a separate set of core symptoms in



**Fig. 1 – Associations of M-ABC-2 overall score (normative mean = 10, standard deviation = 3) and gait variability (a: stride velocity; b: stride time; c: stride length) for children with infantile/atypical autism and controls. Standardized regression coefficients ( $\beta$ ) and  $p$  values are presented next to the slopes. M-ABC-2 = Movement Assessment Battery for Children, 2nd edition. CV = Coefficient of variation.**

the *Diagnostic and Statistical Manual of Mental Disorders*,<sup>1</sup> increasing research highlights common behavioral, cognitive, and neural features.<sup>56</sup> One of the shared neural features is a delay in brain maturation in prefrontal structures,<sup>57–59</sup> which, among other things, include higher order motor control regions.<sup>57,58</sup> As we identified an age-related loss of gait variability in children with infantile/atypical autism and a recent study found a similar developmental pattern in children with ADHD,<sup>41</sup> one could speculate that this common maturational process in gait regularity may be associated with a delayed maturation of frontal brain regions found for both ASD and ADHD.<sup>57–59</sup> However, another brain region that



**Fig. 2 – Associations of age and gait variability (a: stride velocity; b: stride time; c: stride length) for children with infantile/atypical autism and controls. Standardized regression coefficients ( $\beta$ ) and  $p$  values are presented next to the slopes. CV = Coefficient of variation.**

consistently exhibits abnormalities such as volume reduction in both ASD and ADHD is the cerebellum,<sup>56</sup> which is importantly involved in motor movement and locomotor activity.<sup>60,61</sup> Future research might further investigate possible associations between brain maturation, structural abnormalities, and gait patterns to better understand the neural underpinning of the here reported alterations and age-dependent decrease in gait regularity among subjects with ASD.

Our study of course has its strengths and limitations. It is an asset of our study that the gait characteristics were assessed using the objective electronic GAITRite system with proven reliability as well as validity<sup>45</sup> and allowing children to wear their normal clothes and shoes during gait assessment. We additionally included a standardized evaluation tool by using

the M-ABC-2 to assess motor skills of children with infantile/atypical autism and controls. This is in accordance with Rinehart,<sup>27</sup> who suggested that due to the clinical heterogeneity of ASD, assessments of motor functioning using standardized measures should be included when investigating gait data. A further strength of our study is the investigation of a homogeneous cohort by including only children with infantile and atypical autism and excluding children with AS or PDD-NOS. Hence, our findings cannot be generalized to children with AS or PDD-NOS and are only representative for patients with infantile and atypical autism. Indeed we think that our findings of altered gait variability in children with infantile and atypical autism could be a specific finding for this kind of patients but the findings are no sensitive characteristics to delimit them from other developmental disorders.

Furthermore, we examined a larger sample than in previous studies on gait in children with ASD and covered a wide age range by including subjects from 4 to 17 years. Nevertheless, our study was based on cross-sectional data, whereas the investigation of maturational patterns related to gait developmental and the objective assessment of infant pre-walking milestones would require future studies following a longitudinal research approach. Furthermore, we analyzed spatiotemporal gait parameters, as the walkway system GAITRite does not take individual walking patterns into consideration (e.g. toe walking) that are often associated with children with ASD,<sup>17–19</sup> nor the qualitative analysis of gait motion, such as head and trunk posturing.<sup>26</sup> Hence, future studies might investigate whether qualitative aspects of gait motion also show associations with motor skills and whether they follow a similar age-dependent improvement to what we found for spatiotemporal measures of gait variability.

As similar results have been shown in studies with regards to ADHD patients and gait variability, the question arises whether these characteristics can also be expected in further types of neurodevelopment disorders and what role does the cognitive development play concerning these specific characteristics. It is a limitation of our study that we were unfortunately unable to explore this theory, as the majority of our patient cohort was unable to complete the needed testing. Finally, due to the small number of children with infantile/atypical autism being medicated in our sample, we could not investigate possible medication effects. This as well as whether similar findings to those obtained in our study would result for drug-naïve subjects with ASD should be addressed in future studies.

Our findings of maturation of gait variability emphasize that in patients with infantile and atypical autism it is very important to focus and detect as early as possible impairments of gross motor functions such as gait abnormalities and to initiate a movement focused therapy (e. g. physiotherapy). In consequence further investigations has to be done on the one hand to verify the effect of early introducing of movement focused therapy and on the other hand to answer the question whether specific autism intervention programs that normally are based on behavior analytic (e.g. applied behavior analysis) or eclectic early interventions have to be enlarged with movement focused therapy.

In sum, this study provides support for a less regular and less stable walking pattern of children with infantile/atypical

autism. Additionally, our findings are the first to indicate that among subjects with infantile/atypical autism, gait variability is associated with motor skills, whereas infant prewalking motor milestones seem not to be associated with later gait development during childhood. Furthermore, our findings are the first to back the theory of an age-related loss of gait variability in children with infantile/atypical autism and hence an increase in gait regularity toward adolescence. Since differences in motor development are not included as primary diagnostic categories for ASD,<sup>1</sup> the findings of this study support the importance of considering motor functioning, including gait parameters, in addition to other developmental skill areas outlined in diagnostic manuals. It is conceivable that, by increasing the awareness of the movement perspective, new insights on ASD could be provided, possibly helping with determining the degree of specificity of deficits and the development of useful tools for diagnosis.<sup>4,15,62</sup>

### Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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### Conflicts of interest

The authors declare that they have no conflict of interest.

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