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From Early Motor Ability to Global Cognitive Development 7 Years after Neonatal Arterial Ischemic Stroke

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Keywords
Developmental trajectory · Independent walking age · Perinatal stroke · Post-early brain injury developmental condition · Neonatal arterial ischemic stroke

Abstract
The developmental condition of children after neonatal arterial ischemic stroke (NAIS) is characterized by cognitive and motor impairments. We hypothesized that independent walking age would be a predictor of later global cognitive functioning in this population. Sixty-one children with an available independent walking age and full-scale intelligence quotient (IQ) score 7 years after NAIS were included in this study. Full-scale IQ was assessed using the fourth edition of the Wechsler Intelligence Scale for Children (WISC-IV). Independent walking age was negatively correlated with full-scale IQ score at 7 years of age (Pearson correlation coefficient of −0.27; 95% confidence interval from −0.48 to −0.01; $p < 0.05$). Early motor function is correlated with later global cognitive functioning in children after NAIS. Assessing and promoting early motor ability is essential in this population.

Introduction

With a birth prevalence of 1/3,000, neonatal arterial ischemic stroke (NAIS) is the leading cause of unilateral cerebral palsy [1]. Beyond motor function, the developmental condition of children after NAIS is also characterized by global cognitive impairments [2]. In our cohort of 100 infants with NAIS, 49% of children displayed impaired oral language, 22% had low academic skills, and 8% had global intellectual deficiency at 7 years of age [2].

An early motor function assessment is known to be able to identify children with a developmental trajectory of cerebral palsy [1]. The early identification of global cognitive trajectories is more challenging. However, the ability to identify early markers of global cognitive impairment is paramount for the initiation of an early intervention and to promote future activity and participation [3]. The independent walking age is the most accessible evaluation of early motor ability and is associated with the general developmental outcomes of both full-term and preterm children [4, 5]. No studies to date have evaluated this

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Table 1. Features of included and non-included children

	Included children (n = 61)	Non-included children (n = 9)	p values[a]
Neonatal features			
Birthweight z-score, median [IQR][b]	0.3 [1.1]	−0.25 [2.9]	0.96
Male sex, n (%)	36 (59)	7 (78)	0.47
NAIS laterality, n (%)			
Left	40 (66)	4 (44)	
Right	18 (30)	4 (44)	
Bilateral	3 (5)	1 (11)	
NAIS arterial territory, n (%)[c]			
Middle cerebral artery	52 (85)	8 (89)	
Anterior cerebral artery	7 (11)	0	
Posterior cerebral artery	4 (7)	1 (11)	
NAIS location, n (%)			
Superficial	45 (73)	4 (44)	
Deep	4 (7)	1 (11)	
Both	12 (20)	4 (44)	
Independent walking age, months [IQR]	14 [4]	NA	
Development at 7 years			
Full-scale IQ score, median [IQR][d]	99 [24]	75 [32]	0.19
Verbal comprehension index, median [IQR]	99 [23]	94 [25]	0.55
Perceptual reasoning index, median [IQR]	102 [25]	77 [25]	0.11
Working memory index, median [IQR]	91 [24]	79 [33]	0.36
Processing speed index, median [IQR]	100 [24]	76 [50]	0.28

IQ, intelligence quotient; IQR, interquartile range; n (%), number of patients (percentage); NA, non-available; NAIS, neonatal arterial ischemic stroke. [a]Mann-Whitney test or Fisher's exact test. [b]According to the INTERGROWTH-21st International Newborn Size at Birth Standards. [c]Two included children had an NAIS involving two arterial territories. [d]Full-scale IQ score was calculated using the four indices of the Wechsler Intelligence Scale for Children – Fourth Edition.

association in children after NAIS. We hypothesized that independent walking age would be a predictor of later global cognitive functioning in children after NAIS.

Materials and Methods

One hundred term babies born in France between 2003 and 2006 and diagnosed with a NAIS were longitudinally followed according to a predefined plan of investigations (AVCnn Study; NCT02511249), as described [2]. Written parental consent was obtained for each participant. The study was approved by the Regional Ethics Committee. A full-scale intelligence quotient (IQ) assessed with the fourth edition of the Wechsler Intelligence Scale for Children (WISC-IV) was available for 70 children at 7 years of age, as described [6]. Independent walking age was a mandatory field in the database and was longitudinally recorded during standardized follow-up at 1, 2, and 5 years of age. Neonatal features and NAIS characteristics recorded prospectively included birthweight, sex, NAIS laterality, NAIS arterial territory, and NAIS location, as described [6]. Birthweight z-scores were calculated using the INTERGROWTH-21st International Newborn Size at Birth Standards application version 1.3.5 (University of Oxford, UK).

The correlation between independent walking age and full-scale IQ was calculated using a Pearson correlation. The Mann-Whitney test and the Fisher's exact test were used to compare the neonatal features and the IQ scores between included and non-included children for continuous and categorical variables, respectively. A sex difference between independent walking age and the full-scale IQ score was assessed using the Mann-Whitney test.

All statistical tests were two-sided, with $p < 0.05$ considered statistically significant. Statistical analyses were performed using GraphPad Prism version 9.4.

Results

Of the 70 children with a full-scale IQ score at 7 years of age, the independent walking age was not available in nine, leaving a final study population of 61 children with both a recorded independent walking age and full-scale IQ score. The descriptive features of the included and non-included children are displayed in Table 1.

The median age for independent walking was 14 months, with an interquartile range (IQR) of 4 months. All included

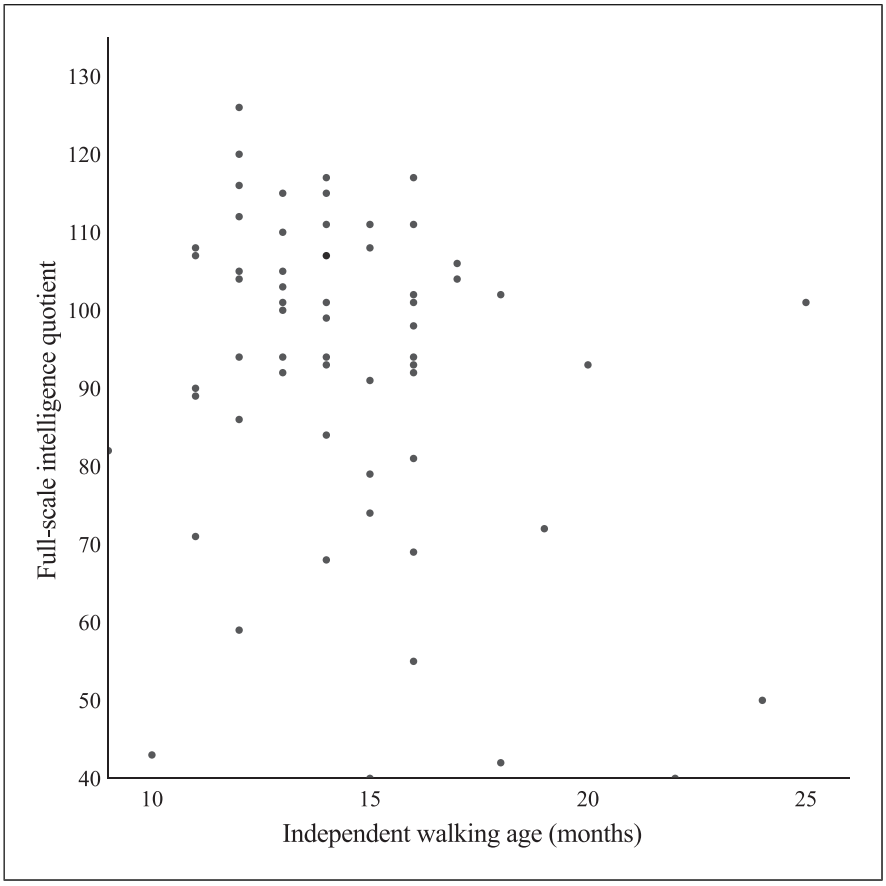

Fig. 1. Independent walking age and full-scale intelligence quotient at 7 years of age.

children achieved independent walking by 25 months of age. The median full-scale IQ score at 7 years of age was 99 (IQR 24). There were no sex differences for independent walking age (median 14 [IQR 3] months vs. 14 [IQR 4] months for males and females, respectively, $p = 0.13$) or full-scale IQ score (median 94 [IQR 24] vs. 104 [IQR 20] for males and females, respectively, $p = 0.09$). The differences in IQ scores between included and non-included children were not statistically significant (shown in Table 1). A negative correlation was observed between the independent walking age and the full-scale IQ score, with a Pearson correlation coefficient of −0.27 (95% confidence interval −0.48 to −0.01; $p < 0.05$) (shown in Fig. 1).

Discussion

An early motor function assessment is correlated with later global cognitive functioning in children 7 years after NAIS. Our study is the first to demonstrate this correlation in children after NAIS. This association between early motor performance and later global cognition has been previously observed in term children with typical development [4], in preterm children [5], and in children with genetic disabilities [7, 8]. The correlation is found regardless of motor proxy: by global observation of the baby (General Movement Assessment), by using validated composite scales based on infant motor patterns (Brunet-Lézine and Bayley Scales), or by determining the age of acquisition for a specific function (walking) [7]. Furthermore, manual tasks such as dexterity are also correlated with global cognition, and the relationship persists years later [9].

There are several possible explanations for these findings. The first is that early sensorimotor experiences will foster future interactions with the world, promote learning and overall development, and eventually generate cognition [7]. Second, even though the stroke lesion is focal by definition, NAIS leads to an extended disorganization of the structural connectome in both lesioned and contra-lesioned hemispheres [10]. We also assume that the diverse constituents of human development (i.e., sensorimotor, language, visuospatial) share common

mechanisms, explaining the high co-occurrence between specific developmental impairments in children after NAIS [2].

Considering this correlation between early motor function and later global cognitive functioning, independent walking age could be regarded as a modulator of the developmental condition of children after NAIS. Age of independent walking could also be a tool for identification of children who could benefit the most from an early rehabilitation program [3].

A limitation of this study is that the independent walking age data were unavailable for nine children out of the 70 with a full-scale IQ score. Nevertheless, in comparing the population that was included and the non-included children, there was no statistical difference in either the neonatal features, NAIS characteristics, or the IQ scores between them. Also, this cohort still represents one of the biggest prospective cohorts of children with NAIS at this age [11].

Early motor function is correlated with later global cognitive functioning in children after NAIS. Assessing and promoting early motor ability is essential in this population.

Statement of Ethics

The study was approved by the Saint-Étienne University Hospital Ethics Committee (IORG0007394). Written informed consent was obtained from each participant.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Antoine Giraud: conceptualization, data curation, investigation, methodology, verifying the underlying data, writing – original draft, and writing – review and editing. Pauline Garel: data curation, investigation, verifying the underlying data, and writing – review and editing. Brian H. Walsh: writing – review and editing. Stéphane Chabrier: conceptualization, data curation, funding acquisition, investigation, methodology, project administration, verifying the underlying data, supervision, and writing – review and editing. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Data Availability Statement

Data are not publicly available due to ethical reasons. Further inquiries can be directed to the corresponding author.

References

1 Dunbar M, Mineyko A, Hill M, Hodge J, Floer A, Kirton A. Population based birth prevalence of disease-specific perinatal stroke. Pediatrics. 2020 Nov;146(5):e2020013201.
2 Chabrier S, Peyric E, Drutel L, Deron J, Kossorotoff M, Dinomais M, et al. Multimodal outcome at 7 Years of age after neonatal arterial ischemic stroke. J Pediatr. 2016 May;172:156–61.e3.
3 Kirton A, Metzler MJ, Craig BT, Hilderley A, Dunbar M, Giuffre A, et al. Perinatal stroke: mapping and modulating developmental plasticity. Nat Rev Neurol. 2021 Jul;17(7):415–32.
4 Walle EA, Campos JJ. Infant language development is related to the acquisition of walking. Dev Psychol. 2014 Feb;50(2):336–48.
5 van Dokkum NH, Reijneveld SA, Bos AF, de Kroon MLA. Attainment of smiling and walking in infancy associates with developmental delays at school entry in moderately-late preterm children: a community-based cohort study. BMC Pediatr. 2021 Feb;21(1):84.
6 Giraud A, Dinomais M, Garel P, Chevin M, Thébault G, Renaud C, et al. Perinatal inflammation exposure and developmental outcomes 7 years after neonatal arterial ischaemic stroke. Dev Med Child Neurol. 2023 Aug;65(8):1073–80.
7 Bos AF. Early neuromotor performance and later cognition in children born preterm. Dev Med Child Neurol. 2021 Aug;63(8):891.
8 Verheyen K, Wyers L, Del Felice A, Schoonjans AS, Ceulemans B, Van de Walle P, et al. Independent walking and cognitive development in preschool children with Dravet syndrome. Dev Med Child Neurol. 2021 Apr;63(4):472–9.
9 Thebault G, Martin S, Brouillet D, Brunel L, Dinomais M, Presles E, et al. Manual dexterity, but not cerebral palsy, predicts cognitive functioning after neonatal stroke. Dev Med Child Neurol. 2018 Oct;60(10):1045–51.
10 Pretzel P, Dhollander T, Chabrier S, Al-Harrach M, Hertz-Pannier L, Dinomais M, et al. Structural brain connectivity in children after neonatal stroke: a whole-brain fixel-based analysis. Neuroimage Clin. 2022;34:103035.
11 Wagenaar N, Martinez-Biarge M, van der Aa NE, van Haastert IC, Groenendaal F, Benders M, et al. Neurodevelopment after perinatal arterial ischemic stroke. Pediatrics. 2018 Sep;142(3):e20174164.