Arch Argent Pediatr 2023;121(3):e202202764

Assessment of general movements in preterm infants as a predictor of cerebral palsy

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ABSTRACT

At present, the early identification of cerebral palsy still poses a major challenge for the health system worldwide. Great advances have been made in neonatology in reducing mortality, but not morbimortality. Cerebral palsy remains the most common sequela of all developmental disorders, especially among those born prematurely. The possibility of early detection before 5 months of age has many benefits for the child and their family, since it allows very early initiation of treatment.

In this study, we describe a highly sensitive and specific tool known as Prechtl's assessment of general movements and its potential complementation with technological apps for early detection.

Key words: *disability/assessment; newborn; motor activity; cerebral palsy; neurodevelopmental disorders.*

doi: http://dx.doi.org/10.5546/aap.2022-02764.eng

To cite: Rosendo N, Vericat A. Assessment of general movements in preterm infants as a predictor of cerebral palsy. *Arch Argent Pediatr* 2023;121(3):e202202764.

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Funding: *None.*

Conflict of interest: *None.*

Received*: 7-5-2022*
Accepted*: 11-1-2022*

INTRODUCTION

By simply observing the behavior of a newborn child in different situations, valuable information can be gained about their development in relation to their gestational age and environmental factors. Infants' ability to self-regulate, their support needs, and behavioral states are expressed through the motor system. Thus, the clinical assessment of an infant's movements has regained momentum, particularly for the detection of cerebral palsy.[1,2]

The objective of this study is to conduct a bibliographic review of new tools for the early detection of cerebral palsy using standardized clinical assessments, such as general movements (GM), and the possibility of combining them with technological apps.

BACKGROUND

Preterm is defined as infants born alive before 37 weeks of gestation and are classified depending on their gestational age.[3]

Advances in perinatal care have prolonged the survival of preterm infants with a very low gestational age, and it is recommended that they enter follow-up programs and are individually assessed in different areas of development.[4]

In Argentina, it is estimated that preterm births account for 10% of all live births and are of great concern to public health, as they are the leading cause of death and comorbidities in children younger than 5 years.[5]

The central nervous system is one of the most affected systems in this population and may develop lesions of varying severity with short- and long-term sequelae. The identification of a potential involvement of the nervous system at an early age has been a challenge for many years in the field of neurology. Its early detection would allow a timely intervention and thus enhance the major neuroplastic changes in the early years, with an improvement in these children´s quality of life.[4,6–8]

NEUROBIOLOGICAL SUBSTRATE OF MOVEMENTS IN EARLY LIFE

Changes in the development of the nervous system in the first year of life allow us to understand the transformation of motor activity in this period. The most significant modifications in the brain occur during the second half of gestation and the first 3 months after birth, particularly in the cortical subplate and the cerebellum. Two phases of development are distinguished in this period: a) the transient cortical subplate phase, mainly present during the first months of fetal life until the first 3 postnatal months, followed by b) the phase in which the permanent circuitries dominate.[9]

This transformation of the brain and cerebellum architecture has a huge influence on the movements observed in preterm infants and may be responsible for neurodevelopmental disorders, such as cerebral palsy (CP), autism spectrum disorders, and attention deficit hyperactivity disorder (ADHD).[10]

This has been proven by histological studies of the cerebral cortex in which the processes of neurogenesis, neuronal migration, and apoptosis have been analyzed, as well as through functional MRIs in resting states in fetuses from 20 weeks postmenstrual age to 38 weeks postmenstrual age, in children in whom the levels of inter- and intra-hemispheric connectivity were studied.[11] In typical development, the integrity of the complex cortical-subcortical networks and the connectivity of the white matter and the transient cortical subplate play a dominant role in the temporary presence of general movements in the last months of gestation and the first 3 months of postnatal life. The cortical activity in the primary sensorimotor cortex shifts from the subplate to the cortical plate leading to changes in connectivity between 3 and 5 months of corrected age. In addition, this structural and functional activity that develops in the brain during the last months of gestation makes it more vulnerable to lesions of all kinds. Hence, it is necessary to use standardized assessments to monitor how these complex processes involved in children's motor development are progressing.[12]

DESCRIPTION OF GENERAL MOVEMENTS. THEIR PREDICTIVE VALUE IN SEVERE NEURODEVELOPMENTAL DISORDERS

From the 8th-10th week postmenstrual age, whole-body movements have been detected by transvaginal ultrasound and dynamic MRI,[13,14] usually performed in pregnant women at 18th gestational weeks onwards. Prechtl, Einspieler, and Marschik have based their work on these and other studies to identify some types of movements, called general movements (GMs), that are distinguished from the motor repertoire of an intrauterine fetus and that exhibit developmental continuity up to 5 postnatal months. These GMs differ from other types of movements performed by the fetus, such as startles, yawns, sucks, hiccoughs, isolated leg and arm movements, among others. They are characterized by being more frequent in occurrence and with more complex patterns, and include a variable sequence of leg, arm, neck, and trunk movements that accelerate and decrease in intensity, strength, and speed with a gradual beginning and end. Rotations around the limb axes and slight changes in the direction of movement make them fluent and elegant and create the impression of complexity and variability. On the other hand, if the nervous system is impaired, these movements loose their complex character and become monotonous and rigid (*Tables 1 and 2*).[2,15,16]

Prechtl and Einspieler suggest that GMs arise from the central pattern generator most likely located in the brainstem and spinal cord, and undergo changes as structures of the cerebral cortex are modified. These modifications are manifested in temporal changes in movements, which are called: a) preterm general movements from postconceptional week 8 to term-age, b) writhing movements in term infants until 6–9 weeks post-term, which gradually disappear to give way to c) fidgety movements, which will be present until approximately 5 months of age, when voluntary and antigravitational movements progressively take control of the movement (*Figure 1*).[2,17,18] The analysis of these GMs has made it possible to use them as a tool to assess their quality due to their ease of use, low cost, and 98% sensitivity in the early detection of motor disorders before 5 months of age when used together with a thorough clinical history of the child.[4,16,18,19]

The procedure for filming and assessing GMs consists of making 1-3 minute long videos, with the child in supine position, spanning the whole body, with the child comfortably dressed in a diaper or very light clothing that allows to observe the child's movements freely. The child should be awake and calm. Then the Gestalt approach is used to analyze the video and movements are categorized, as recommended by Prechtl and Einspieler, into normal and abnormal, as mentioned in *Table 1*.[2,15,16]

Table 1. Characteristics of writhing movements between 20 and 46 weeks postconception

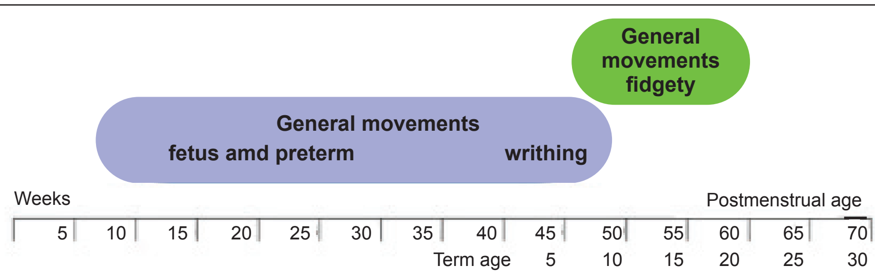
Normal	•	Complex, involving the whole body with rotations
	•	Fluent, with gradual onset and end
	•	Variable in terms of strength and speed
Abnormal	•	Poor and monotonous repertoire
	•	Synchronized stiffness, non-fluent, jerky
	•	Chaotic

Table 2. Characteristics of fidgety movements between 9 and 20 weeks post-term

Normal	•	Small range and moderate speed
	•	Variable acceleration in 3 plane
	•	Semicircular wrist and ankle movements
	•	Involving the whole body, head, and trunk
Abnormal	•	F-: absence of normal fidgety movements
	Å	F+: very exaggerated range and speed

F-: does not express normal movements; F+: expresses very exaggerated movements.

Figure 1. Temporal development of general movements



RELEVANCE OF SEVERE MOTOR DISORDERS IN PRETERM INFANTS

Preterm infants have motor, sensory, and behavioral comorbidities when compared to full-term infants. Among motor disorders, there is a higher prevalence of cerebral palsy, and this risk increases with decreasing gestational age.[20] The main cause is encephalopathy of prematurity, which causes sequelae and is responsible for 5% to 25% of preterm infants with motor deficits.[8,21] Encephalopathy of prematurity is caused by lesions in the periventricular white matter and is frequently accompanied by lesions in the cerebellum, thalamus, basal ganglia, and brainstem, in a combination of primary destruction and impairment of trophic mechanisms.[22]

Currently, there is broad consensus on the advantages of early diagnosis in this population, that makes it possible to provide early intervention programs within the first year of life. This recommendation is based on the fact that, on the one hand, at this stage, the brain is in a period of major structural and functional changes and has great potential to offset the sequelae due to the enormous brain plasticity. On the other hand, early detection is intended to provide support to the families who need guidance and participation in the upbringing of their children.[7,8,23]

ADVANCES IN THE EARLY DETECTION OF CEREBRAL PALSY

Cerebral palsy is the most common disability in childhood, with varying prevalence worldwide. It encompasses a group of syndromes that cause permanent developmental disorders of movement and posture, and activity limitations, and are attributed to non-progressive disturbances that occurred in the development of the fetal or infant brain. These disorders are often secondary to brain lesions or abnormalities, arise in the early stages of development, modify their expression, and cause limitations in the child's performance and activities of daily living.[24]

Diagnosis continues to be based on clinical findings; in some cases, it is complemented with neuroimaging and, in other few cases, with metabolic and/or genetic studies[4,25] because the etiology is unclear in 80% of cases. New evidence suggests that 14% of all children with CP have genetic alterations of their own.[26]

Regarding advances in molecular and genetic studies, new evidence suggests that epigenetic markers related to the psychosocial, chemical, physical, and environmental setting to which the mother and child are exposed are also predictive and conditioning of neurodevelopmental outcomes as, in the long run, they may lead to deleterious effects on the developing brain.[1,26]

In a multicenter study published by Novak et al., they found that the 3 tools with the highest predictive validity for detecting CP are, firstly, Prechtl's qualitative assessment of GMs with a 98% sensitivity,[16,17] described above; secondly, the Hammersmith Infant Neurological Examination (HINE) with a 90% sensitivity; and, thirdly, the neonatal MRI with an 86-89% sensitivity.[4,27,28]

The HINE is a standardized assessment tool which consists of 26 easily replicable items for assessing children between the ages of 2 and 24 months. Its score ranges between 0 and 78, and is highly predictive of CP at 2 years old. This scale may be combined with the assessment of GMs at 3 months of age, which further improves the results to predict CP.[4,29] Regarding the use of MRI as a method, it can be performed up to 3 months of age during the child's natural sleep or with a dose of sedation and wrapped in its sleeper nest; after 3 months of age, general anesthesia is required.[29]

PROSPECTS FOR THE ASSESSMENT OF GENERAL MOVEMENTS COMBINED WITH THE USE OF TECHNOLOGY

In recent years, video analysis has been developed by means of different computational applications in conjunction with the assesment of GMs and using advances in what is known as deep learning (DL) and artificial intelligence (AI). Regarding these new possibilities, there is still no standardized approach of using both DL and AI, nor a consensus regarding which are the most convenient forms of recording.

There are other publications using different methodologies to process videos. Some methodologies imply placing a suit or breastplate with sensors on the child; others only place bracelets with sensors on the skin of the wrists and ankles mapping key points of the child's body,[30] and in other cases 2D analysis is used with cameras that track body parts and characteristics of movement patterns that are then processed by algorithms.[31,32]

Finally, experiences have been published in which they have used smartphone apps. Based on this technology, Adde L. et al. created an app called In Motion, which they installed on the phone of a control group of 86 parents. This app tracks 7 key points on the child's body and then the medical team processes the data obtained from the accelerometers included in the software, and analyzes the GMs collected by the parents.[33] In another study, Spittle proposes the assessment of preterm infants by using another smartphone app. Parents are asked to film their children for further analysis on the basis of the quality of movement.[34]

DISCUSSION

Based on our review and personal experience studying GMs and using data tracking software, we believe that this type of video analysis tools, as Silva et al. have described,[30] are not yet capable of distinguishing, as the human eye does, between different types of abnormal movements, and this undermines their prognostic value.[35] Obtaining good results in the short- and medium-term using AI seems to be very risky in spite of the attempts made, since these procedures are time-consuming, and require a lot of technological and economic resources, in contrast to the traditional possibility of being able to draw conclusions after watching a short video. It should be noted that sample sizes in studies carried out using DL and AI are small, significant financial and technological support has been required for conducting them, and this limits us greatly in our setting, in addition to the fact that even the apps downloaded to phones are for closed use by researchers and not for free use. It is very likely that human analysis of videos will continue to be used for some time in the assessment of GMs and better and better large-scale outcome are expected from software programs that could analyze a large number of videos.

CONCLUSIONS

We believe that, in the coming years, the challenges will lie in improving the accuracy for the early detection of high risk children and maintaining the communication between developmental experts and computer engineers to ensure the reliability of future mathematical models.[30]

Future use of a combination of standard assessments and large-scale DL or AI would facilitate the early detection and implementation of early intervention programs in children. This could benefit both children and their families, from the first months of life, by providing counseling and implementing them as a key part of their children's treatment, as well as reducing stress and improving mental health. ■

Acknowledgments

We would like to thank Viridiana Pistorio and Ramilo Freudhenthal for their valuable contributions to the manuscript.

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