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GENERAL MOVEMENT ASSESSMENT IN EARLY DIAGNOSIS OF NON-PROGRESSIVE CHRONIC ENCEPHALOPATHY OF CHILDHOOD

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Abstract: **Introduction:** Chronic Non-Progressive Encephalopathy of Childhood (ECNPI) refers to the group of non-progressive sensorimotor impairments secondary to damage to the Central Nervous System during an early stage of development. Its diagnosis is usually made between 18 and 24 months of age, when the infant demonstrates significant disabilities. Additionally, complementary exams are necessary, which increase the cost and delay the diagnostic process. The *General Movement Assessment* (GMA) allows the early diagnosis of ECNPI, which can optimize the initiation of physiotherapeutic treatment. **Objective:** To carry out an integrative review of the literature on the use of GMA in the early diagnosis of ECPNI. **Results:** A review was carried out containing articles from systematic or simple reviews and clinical trials, in English and Portuguese, published between 2011 and 2021 or with a number of citations greater than 40, in Google Scholar Pubmed and PEDro databases. Ten articles that evaluated GMA in the early diagnosis of ECNPI were included, with their methods and results tabulated. **Conclusion:** The literature suggests the use of GMA because it has low cost and high predictive values, specificity and diagnostic sensitivity for ECNPI. The GMA must be incorporated into newborn assessment routines, especially high-risk ones.
Keywords: Motor activity; early diagnosis; Cerebral Palsy.

INTRODUCTION

Chronic Non-Progressive Encephalopathy of Childhood (ECNPI) or Cerebral Palsy (CP) are terms used to name a group of disturbances in sensorimotor development, non-progressive, but changeable (STOEN et al., 2019), resulting from lesions in the Central *Nervous* System (CNS), which can be caused in the pre, peri or postnatal period (SEME-CIGLENEÈKI, 2003). It is the most frequent cause of motor impairment, usually diagnosed between one and two years of age, when the infant begins to show significant impairments in gross motor, sensory and/or cognitive function (PHILIPPI et al., 2014).

Early diagnosis is defined as an early identification of some condition, without the first signs and symptoms of a syndrome (SEME-CIGLENEÈKI, 2003). In children with ECNPI, it allows starting an orientation program for those responsible, preventive clinical treatment, sensorimotor, cognitive and functional stimulation, before a comorbidity resulting from the underlying pathology sets in. This type of approach can alleviate possible motor dysfunctions, allow the adaptation of activities and functions for greater independence of the child, thus contributing to their development. In children with ECNPI, it is important that the diagnosis be made before the second year of life, as this is the period of better neuroplasticity and greater motor, cognitive and expressive acquisition. Currently, the diagnosis of ECNPI depends on carrying out several tests, both laboratory (to rule out other causes of the child's clinical condition) and neuroimaging, which increases the cost and delays the diagnosis, making early intervention unfeasible (MORGAN et al., 2019).

The *General Movement Assessment* (GMA) is a qualitative observational assessment instrument, which allows an early diagnosis of ECNPI from the first weeks after birth to 5 months of age, through the general and spontaneous movements that newborns (NBs)) and infants reproduce (EINSPIELER *et al.,* 2013). GMA is a low-cost, non-invasive, fast strategy (which does not generate stress for the subject) and has high sensitivity and diagnostic reliability (AKÇAKAYA *et al.,* 2019), allowing the prognosis of neurological development to be made before the first signs of spasticity (SEME-CIGLENEÈKI, 2003)

The movements assessed by the GMA are divided into *Writhing Movements (WMs)* and *Fidgety Movements (FMs),* according to the age of the NB or infant. WMs start from fetal age to the eighth week after birth. From six to nine weeks, these movements gradually disappear and the FMs start, lasting until the fifth month (time when the CNS maturation occurs) (EINSPIELER & PRECHTL, 2005). These movements allow an evaluation that optimizes the beginning and focus of the physiotherapeutic treatment (AKÇAKAYA *et al,* 2019). The most striking feature of these movements is that they are composed of a variable sequence of trunk, neck, arm and leg movements with varying speed and intensity, being complex and smooth movements (EINSPIELER et al., 2013).

General *Movements (*GMs) are classified as: *"poor-repertoire"* (poor repertoire), which consists of monotonous movements; *"Cramped-Synchronized" (synchronized cramps), which are* rigid movements in which all the muscles of the limbs and trunks contract and relax simultaneously; *"Chaotic"* (chaotic), which are uncoordinated movements without fluency; *"Abnormal Fidgety Movements",* which are abnormal FMs, that is, with exaggerated amplitude, speed and complexity; and, *"Abstance of Fidgety Movements"* when FMs are not perceived (EINSPIELER & PRECHTL, 2005).

Although it is very sensitive and specific for the diagnosis of ECNPI, the GMA is still not widely used in clinical practice as an evaluation tool. In this sense, the objective of this study was to carry out an integrative literature review on the use of GMA in the early diagnosis of Non-Progressive Chronic Encephalopathy of Childhood. And, secondly, to discuss the use of the GMA in the early diagnosis of children with Non-Progressive Chronic Encephalopathy of Childhood, in addition to describing its applicability, reliability and sensitivity.

METHODOLOGY

This is an integrative literature review, in which systematic or simple review articles and clinical trials were used, both in English and in Portuguese, published between 2011 and 2021, obtained from June to September 2021., from the Pubmed, Google Scholar and PEDro databases, using the following keywords: "General *Movement Assessment"* and *"Cerebral Palsy"*. Some articles, although published before 2011, were selected due to the importance of their content and the high number of citations (greater than 40 citations). Thus, the process of search and selection of articles followed the following steps: (1) search for articles according to keywords; (2) reading of abstracts; (3) application of inclusion criteria; (4) reading the articles in full; (5) inclusion of selected articles.

RESULTS

Initially, from the search in the databases by keywords, 710 articles were found. After applying the inclusion criteria, 27 articles were selected. After reading the abstracts, only 23 mentioned the GMA in the ECNPI. Of these, only 10 articles met the work demand of talking about GMA in the early diagnosis of ECNPI, evidencing its sensitivity, specificity and applicability (Figure 1). Table 1 presents the articles that suggest the applicability of the GMA, both in NBs and in infants up to 5 months old, for the early diagnosis of ECNPI.

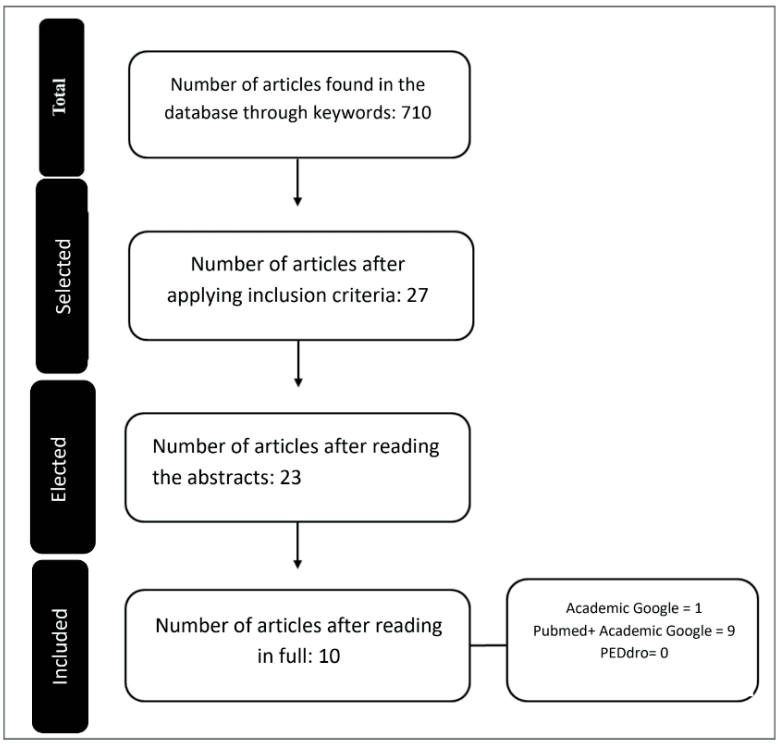

FIGURE 1: Article selection process

AUTHOR/ YEAR	TITLE	METHODOLOGY	RESULTS	CONCLUSION
Wang *et al.*, 2020	Establishing an early identification score system for cerebral palsy based on detailed assessment of general movements.	Case study with 114 babies, where the GMA and a detailed score were applied, at the age of WM (4-6 weeks) according to different developmental outcomes based on the tests: neuromotor (evaluates passive muscle tension, motor activity and reflexes); and Gesell development scale (applied to identify motor delays through DQ). Follow-up outcome was determined at month 12 according to ECNPI diagnostic criteria.	The GMA with this detailed score demonstrated a predictive value of 92.11%, with a sensitivity of 100%, specificity of 90%, having a PPV of 72.73%, NPV of 100%, indicating a rate of 0 false negatives and 10% false positive.	The GMA based on the WMs is correlated with clinical neurological examination and allowed the early diagnosis of infants with ECNPI, who were referred for early intervention.
Stoen *et al.*, 2019	The Predictive Accuracy of the General Movement Assessment for Cerebral Palsy: A Prospective, Observational Study of High-Risk Infants in a Clinical Follow-Up Setting.	Clinical study comprising 450 high-risk infants that started in the FM phase and lasted up to 18 to 24 postnatal months. The study verified the accuracy of GMA alone and in combination with neuroimaging exams. The FM were classified by two *GM Trust* certified observers (advanced level) who did not have access to the infants' clinical history.	42 children were diagnosed with ECNPI. The predictive value of absent or sporadic FMs of ECNPI had a sensitivity of 76.2% and a specificity of 82.4%. Only three out of 37 babies with sporadic FM developed ECNPI. The greatest diagnostic accuracy for the development of ECNPI was achieved by a combination of absent FM with atypical neonatal imaging.	The combination of GMA with neuroimaging exams allows for more specific results. Absent or poor FM are important landmarks for the early diagnosis of ECNPI. In addition, they allow identifying the possible occurrence of autism and other developmental disorders.

Morgan *et al.,* 2019	The Pooled Diagnostic Accuracy of Neuroimaging, General Movements, and Neurological Examination for Diagnosing Cerebral Palsy Early in High-Risk Infants: A Case Control Study.	Retrospective study, with 441 control cases (147 diagnosed with ECNPI, 147 with mild deficiency without ECNPI and 147 typical). We retrieved HINE and GMFCS scores, GMA assessments, and neuroimaging data (MRI or USG) in children with ECNPI to assess the early predictive value of ECNPI.	HINE showed a sensitivity of 88% and a specificity of 62% for the detection of ECNPI, GMA showed 95% sensitivity and 97% specificity, while neuroimaging exams showed 79% sensitivity and 99% specificity. The predictive value of the three combined assessments gave a sensitivity of 97.86% and specificity of 99.22%, with a PPV of 98.56% and a NPV of 98.84%.	The predictive value of GMA in combination with neuroimaging and HINE was highly accurate for early detection of ECNPI. The combined sensitivity and specificity of the three instruments together were greater than the three tools alone.
Akçakaya *et al.*, 2019	Correlation of Prechtl Qualitative Assessment of General Movement Analysis with Neurological Evaluation: The Importance of Inspection in Infants.	Cross-sectional and retrospective study, consisting of 80 neonates aged less than 20 weeks. The sensitivity and specificity of the GMA was investigated and its results were compared with neurological assessments.	The GMA predicted delay in neuromotor development with a sensitivity of 95.8% and a specificity of 87.3% and FMs were shown to have a sensitivity and specificity of 97% and 90.4% respectively, with a post term age of 9- 20 weeks best for evaluation.	GMA proves to be an important screening method for early diagnosis, in addition to ECNPI, motor deficits in early childhood due to its high correlation with neurological examinations.
Eispieler *et al.,* 2019	Cerebral Palsy: Early Markers of Clinical Phenotype and Functional Outcome.	Observational clinical study, with a sample of 468 children who received a diagnosis of ECNPI. The GMA was used when infants were 9 to 22 weeks post-term and was administered by 1-5 *GM Trust certified scorers* (advanced level) to identify specific early markers for future limitations in gross motor function.	95% of children with ECNPI did not have FM, and all of them had non-ideal MOS. Asymmetrical segmental movements were strongly associated with unilateral ECNPI, while circular arm movements were associated with dyskinetic ECNPI.	The GMA is capable of early identification of ECNPI (with a sensitivity of 94% and specificity of 92%). The use of MOS contributes to the understanding of the later prognosis of ECNPI, including early markers for type and severity. Absence of FM may be associated with low MOS but does not predict GMFCS score. For an accurate diagnosis, it is necessary to use MRI, but it is a costly resource.
Darsaklis *et al.*, 2011	Predictive validity of Prechtl's Method on the Qualitative Assessment of General Movements: a systematic review of the evidence.	Systematic review with longitudinal cohort study for the predictive validity of the *Prechtl method* in GMA with regard to neurodevelopmental outcomes. All articles that reported on the predictive validity of the GMA were used. Studies were separated according to follow-up age: 12 to 23 months; 2 to 3 months; 4 to 11 months; and 12 to 18 years old.	39 articles were evaluated. Sensitivity, specificity, PPV and NPV values varied between studies. Studies have indicated that the presence of quality abnormalities in FMs (at 12 weeks corrected age) is more predictive of adverse outcomes than in abnormal WMs.	The GMA is a high-quality, low-cost, non-invasive tool, with sensitivity ranging between 75-100% and specificity between 40-84% for the early diagnosis of ECNPI and other coordination disorders. It is important that neuroimaging exams and clinical evaluation are performed in association with the GMA.

Adde *et al.*, 2010	Early prediction of cerebral palsy by computer-based video analysis of general movements: a feasibility study.	Cross-sectional study involving 30 high-risk infants (mean gestational age 30 weeks). FMs were assessed from video recordings in infants between 10- and 15-weeks post-term. Movement tracking sensors were attached to the extremities, sternum and frontal region of the evaluated infants. After 4-7 years, babies were evaluated by a multidisciplinary team.	Thirteen infants developed ECNPI. Of these, 12 had absent FM. The 13 children were classified according to the type of ECNPI (8 with spastic hemiparesis, 4 with spastic quadriparesis, 1 dyskinetic) and it was possible to identify the functional level of 10 children.	The GMA had a sensitivity of 85% and a specificity of 71% in identifying ECNPI and, when associating it with variables that reflect the amount of movement, the specificity increased to 88%. Combining the variables amount of movement and standard deviation of speed, it can be predicted for most children whether they would be able to walk or not.
Adde *et al.*, 2007	General movement assessment: Predicting cerebral palsy in clinical practice.	Cross-sectional study with 74 babies (term and preterm). Neuroimaging exams were collected from all high-risk infants in the neonatal period. The GMA was applied between 10- and 18-weeks post-term (FM period). Babies with congenital syndrome and malformations were excluded from the study. All recordings were performed and graded by the same physiotherapist (certified by the GMA *Trust)*, who also had knowledge of the babies' medical history. Recordings were made for at least 30 minutes after feeding and lasted for several minutes during periods of active wakefulness. The presence or absence of ECNPI was reported at 23 months of corrected age. Each child's neurological outcome was classified into three groups: ECNPI, non-ECNPI, or unclear. Data from neurological examination results were compared with the GMA.	Of the 74 infants evaluated (25 classified as high risk), 10 developed ECNPI and 3 outcomes were uncertain. Of the 49 babies classified as low risk, none developed ECNPI. Comparison of the GMA with the results of neurological examinations showed that of 13 babies with abnormal FM, 10 developed ECNPI, 2 were uncertain and 1 did not. And of those with normal FMs (61), sixty did not develop ECNPI and 1 outcome was uncertain.	GMA is effective for an early diagnosis of ECNPI, with 95% sensitivity and 95% specificity. It is believed that in lighter ECNPI the GMA results are not so reliable, requiring further studies. It is suggested that the evaluation criteria of general movements be more objective and standardized.

Eispieler & Prechtl, 2005	Prechl's assessment of general movements: a diagnostic tool for the functional assessment of the Young nervous system.	Bibliographic review that described the general and spontaneous movements of the baby.	The specificity of the same studies was lower during the movements of preterm and WM infants (46% to 93%). This was attributable to the number of babies with abnormal GMs (mainly poor repertoire) at this early age who normalized before or during the FM period. With increasing age, specificity increased revealing values between 82% and 100% during the third month, when normal FM predicts a normal neurological outcome.	It is believed that GMA predicts the later development of ECNPI early, before pathological features, in addition to being a totally non-intrusive technique, easy to learn and cost-effective.
Seme-Cigleneeki, 2003.	Predictive Value of Assessment of General Movements for Neurological Development of High-Risk Preterm Infants: Comparative Study.	Randomized clinical study, in which 232 high-risk babies, with gestational age less than or equal to 37 weeks, participated. These were divided into two groups: the study group, in which the GMA and the classic neurological examination were performed, comprising 120 infants; and the control group, composed of 112 infants who underwent only the neurological examinations. The GMA was performed when the infants were 3 months of corrected age, while the neurological examinations were performed at 3, 12, 18, 21, and 24 months of corrected age. All babies had their neuropsychomotor development evaluated at 24 months of corrected age, when it was possible to confirm the diagnosis of ECNPI.	The GMA results obtained when the baby was 3 months corrected age were compared with his neurological exams at 24 months. The GMA had fewer false negatives and false positives than the neurological exam, obtaining 92% validity, 94% sensitivity, 92% specificity, 81% PPV and 98% NPV. While the neurological examination showed validity of 60%, sensitivity of 97%, specificity of 43%, PPV of 44% and NPV of 95%.	The GMA proved to be a method with high reliability, validity, sensitivity and specificity. The GMA performed early detection of ECNPI in children with a gestational age of 3 months, before the first signs of spasticity.

ECNPI = Chronic Non-Progressive Encephalopathy of Childhood; DQ: Development quotient; FM: Fidgety *Movement*; GM: General Movement; GMA: General Movement Assessment; GMFCS: Gross Motor Function Classification System; HINE: *Hammersmith* Neurological Assessment; MOS: *Engine Optimality Score*; MRI: Magnetic Resonance; USG: Ultrasonography; NPV: Negative Predictive Value; VPP: Positive Predictive Value WM: *Writhing Movements*

TABLE 1: Characteristics of the articles selected in this review

DISCUSSION

The main objective of this study was to carry out an integrative literature review on the use of the *General Movement Assessment* in the early diagnosis of Non-Progressive Chronic Encephalopathy of Childhood. And, secondly, to discuss the use of the *General Movement Assessment* in the early diagnosis of children with Non-Progressive Chronic Encephalopathy of Childhood, in addition to describing its applicability, reliability and sensitivity. Through the application of

selection and eligibility criteria, 10 articles were included in this integrative review. The methods and results of each article were tabulated and their methodologies and main outcomes will be discussed below.

Authors Wang *et al.* (2020), described the GMA as an important clinical screening tool for the early prediction of ECNPI. These authors agree with Seme-Cigleneèki (2003) and Einspieler & Prechtl (2005) who also describe the GMA as a sensitive method to predict ECNPI according to the general and spontaneous movements that infants reproduce, adding that the GMA is a non-invasive, low-cost and easy-to-learn technique. Adde *et al.* (2007) bring in their study that GMA is a sensitive method to predict neurodevelopmental disorders including ECNPI. Studies on the predictive value performed in combination with other neurological exams, whether clinical (such as the Hammersmith Neurological Assessment - HINE) and/or neuroimaging (magnetic resonance imaging and ultrasound) for the prediction of ECNPI, were commented by the authors Seme-Cigleneèki (2003), Adde *et al.* (2007), Eispieler *et al.* (2013), Morgan *et al.* (2019) and Stoen *et al.* (2019), showing that, together, they contribute to the accuracy of this diagnosis, and, on the other hand, with a higher cost. In addition, these exams depend on the GMA result up to 24 months for an accurate early diagnosis. Akçakaya *et al.* (2019) shows the high correlation of GMA with neurological examinations.

Positive predictive value (PPV) is the probability that an individual evaluated with a positive result is really sick and negative predictive value (NPV) is the probability that an individual evaluated with a negative result is really typical (ie, does not have the pathology). In studies by Seme-Cigleneèki (2003) and Wang *et al.* (2020), NPV values were shown to be significantly higher than PPV, which brings reliability to the GMA method, proving to be an important screening tool for the early prediction of ECNPI. The sensitivity and specificity of GMA described in the articles by Seme-Cigleneèki (2003), Adde *et al.* (2007), Eispieler *et al.* (2013), Akçakaya *et al.* (2019) and Stoen *et al.* (2019) ranged from (systematic reviews were not taken into account) 76.2% (STOEN et al., 2019) -100% (ADDE et al., 2007) (value similarity between the systematic review by DARSAKLIS et al, 2011) and 82.4% (STOEN et al., 2019) -98% (ADDE et al., 2007), respectively. Both applied the GMA during the FM period. The explanation for the lower values of sensitivity and specificity is attributed to the study carried out by Stoen *et al.* (2019) is that fewer infants were confirmed with ECNPI (42 babies) compared to the study that gave a higher sensitivity and specificity value in the study (ADDE et al., 2007), with 74 babies confirmed. Having a high sensitivity and specificity means that the GMA allows differentiating babies that will possibly develop ECNPI and those that will not present the disease with a small margin of error.

Some studies were carried out to compare the GMA with neuroimaging exams and other pediatric clinical exams: in Seme-Cigleneèki (2003), classic neurological exams with sensitivity and specificity of 97% and 43% respectively and with PPV of 44% and NPV of 97%; and in Morgan *et al.* (2019) were found to be less specific regarding GMA with HINE showing sensitivity of 90% and neuroimaging exams showing sensitivity and specificity of 86% and 89%, respectively.

Eispieler *et al.* (2013), explained that the detailed analysis of the GMs and the posture of the infants provides markers that are associated with the severity and location of the ECNPI, allowing the subsequent prognosis of this child. Stoen *et al.* (2019), Einspieler *et al.* (2019), and Wang *et al.* (2020) demonstrate

that it is possible to predict the severity and type, as well as predict the level of the Gross Motor Function Classification System (GMFCS). Eispieler *et al.* (2019), describe a way in which higher scores (greater than 14 points) would be indicative of a GMFCS I or II (preserved ambulatory functions) and a score lower than 8 points indicates a GMFCS IV and V (non-ambulatory). This score has a sensitivity of 95% and a specificity of 98%.

In another study that investigated the impacts on motor function, Wang et *al.* (2020) evaluated passive muscle tone, motor activity for a detailed score showing that the higher it is, the greater the indicative for NECNP and with greater future motor impairment showing the predictive value of 92.11%, sensitivity of 100%, 90% specificity, with 0% false negatives and 10% false positives. What made these methods viable and accessible. Through his study, Seme-Cigleneèki (2003), concluded that absent or abnormal FMs are strong predictors for the early prediction of ECNPI, and normal FMs are strong indicators of future normal neurological development. Morgan *et al.* (2019) also comments on the importance of prognosis for prior intervention to minimize the development of side effects and maximize motor and cognitive effects, optimizing neuroplasticity, preventing complications and providing adequate psychological support to parents.

Gestalt observation and video analysis, Adde *et al.* (2010) decided to apply the GMA through video recording and install three-dimensional electromagnetic sensors, which allowed identifying the functional level of most of the infants observed. Given this, Adde *et al.* (2010) applied the GMA through a computerized kinematic analysis and compared it with the clinical *Gestalt analysis* and observed that these two evaluations taken together would be more accurate in the early diagnosis. This study proved that the video analysis by the GMA becomes more specific and able to predict the ECNPI being ambulatory or not and the level of the GMFCS. Finally, the GMA can be analyzed by video and remotely, directly interfering with the prognosis of this child so that an early intervention is carried out, which, according to Einspieler et al. (2013), reduces the negative effects caused by damage to the functional abilities of these children.

CONCLUSION

The General Movement Assessment (GMA) has shown to have a high positive and negative predictive value, with high sensitivity and specificity, proving to be a low-cost, easy-to-apply and reliable tool for the early diagnosis of Chronic Non-Progressive Encephalopathy of Childhood (ECNPI), before 2 years of age (for example: before the first characteristic clinical signs of ECNPI). The GMA also contributes to establishing the prognosis of a child with ECNPI, allowing an educational, preventive and early interventionist approach.

Although more studies are needed to contribute to the evidence of the use of GMA in the early diagnosis of ECNPI, the GMA can and must be incorporated into routine assessment of NBs, especially preterm infants at high risk for developing ECNPI.

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