General movement assessment is correlated with neonatal behavior neurological assessment/cerebral magnetic resonance imaging in preterm infants

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Abstract
To explore the relationship between general movements (GMs) and neonatal behavior neurological assessment (NBNA)/cerebral magnetic resonance imaging (MRI) in preterm infants.
Forty preterm infants were examined with GMs assessment before gestational age of 40 weeks; NBNA was performed at the age of 40 weeks; cerebral MRI was performed at the age of 42 weeks.
Our experiment showed that preterm infants with poor GMs scores are more likely to have low NBNA scores (P = .001); preterm infants with abnormal cerebral MRI are more likely to have low NBNA scores (P = .002); preterm infants with poor GMs scores are more likely to have abnormal cerebral MRI (P = .012).
GM assessment is correlated with NBNA and MRI results in preterm infants for neurological development.

Abbreviations: GMs = general movements, MRI = magnetic resonance imaging, NBNA = neonatal behavior neurological assessment.

Keywords: cerebral magnetic resonance imaging, general movement assessment, neonatal behavior neurological assessment, preterm infants

1. Introduction
With the advances in neonatal intensive care unit, the preterm infants, including very low birth weight survival rate has significantly improved. However, there are some conditions with poor prognosis, including permanent head damage, intellectual disability, and seizures.[1] Therefore, it is essential to diagnose neurological development abnormalities for early interventions.

Traditional magnetic resonance imaging (MRI) is a commonly used clinical tool for early diagnosis and prediction. Abnormal images were found in 83% brain paralysis patients.[2] Neonatal behavior neurological assessment (NBNA) as invented by Dr Xiulan Bao based on the modification of Brazelton neonatal behavior assessment (US) and Amiel-Tison neurological assessment (France).[3] NBNA is suitable for neurological injuries early screening and evaluation. General movements (GMs) assessment is a newly developed evaluation tool for brain function, its high sensitivity towards neurological injuries and early prediction makes it valuable.[4]

In the current study, we performed GMs and NBNA, brain MRI in 40 preterm infants. We further analyzed the correlation between these 3 measurements. Our results provided an important clinical tool for neurological development abnormalities.

2. Methods
2.1. Study population
Subjects enrolled Nantong University Affiliated Hospital neonatal intensive care unit from January 2014 to June 2014. Enrollment criteria: weight < 2.5 kg; gestational week < 34 weeks at birth; within the first 30 days of life. Exclusion criteria: congenital malformations; genetic syndromes; respiratory distress severe enough that they were not expected to live (oxygenation index, ≥20); other underlying diseases (such as congenital heart disease). This study was approved by the ethics committee of Affiliated Maternity and Child Health Care Hospital of Nantong University on October 15, 2013 (Y2013016), and oral informed consents were obtained from the legal guardians for all subjects.
2.2. GMs assessment

GMs were divided into 2 phases in development. Neonatal phase and twist movement (postnatal till full term 8 weeks), with complicated movements. Unsteady movement phase (full term 9 weeks to 5 months), with gentle and mild speed movement. The infants were videoed for assessment of twist movement as previously described. In brief, during the recording, the infants were supine on the incubator, crib or mat, wearing standard filming clothes, keeping active and awakened, and avoiding crying, irritability, continuous hiccups, or using a comfort pacifier. The recording lasted for 5 to 10 minutes. The videos were assessed by clinicians with certification in GMs assessment. During the assessment, the video audio signal was turned off, and the GMs were assessed using Gestalt perception to distinguish between normal and abnormal, then further classified as poor repertoire, cramped-synchronized, or chaotic. Abnormal GMs were recorded as positive.

2.3. NBNA

NBNA included 5 parts, behavioral ability (6 items, including response to light stimulus, “panic” response, face reaction, reaction to red ball, and comfort reaction), passive muscle tension (4 items, including scarf sign, forearm Bounceback, axillary angle, and rebound of lower limbs), active muscle tension (4 items, including active contraction of the neck flexors and extensors, hand holding, traction response, and supportive erectile position), primitive reflexes (3 items, including sucking motion, embracing reactions, and stepping or placing responses), and general evaluations (3 items, including arousal, crying, and activity). Each score has 3 divisions: 0 points, 1 point, and 2 points. The total was 40 points. Abnormal NBNA was defined as <35. The evaluators were medical personnel who have been working in children’s health care for a long time with certification. The assessment time was 2 weeks after full term.

2.4. Cranial MRI

A Siemens Open 0.2T MRI system (Siemens, Berlin, Germany) was used to routinely perform fast spin echo T2WI, spin echo T1WI, and sagittal T1WI on the transverse axis. Some case-sex sagittal T2W and coronal T1WI examinations, matrix 240 × 256 mm, thick layer 6mm. Twenty minutes before the examination, 10% chloral hydrate 50mg/kg enema was given, and 2 or more high-level doctors engaged in the specialty were in charge. The cranial MRI image showed any sign of structural abnormality in the brain as a positive result, and a score that was consistent with the characteristics of the brain structure of this age group was considered negative. The evaluation was performed after full term.

SPSS13.0 (SPSS Inc, Chicago, IL) was used to perform all the statistical analysis, and Spearman test was used to compare the 3 groups.

3. Results

A total of 40 cases were included in the study. There were 24 males and 16 females. The gestational age ranged from 26 weeks to 34 weeks, including 26 weeks to 28 weeks (3 cases), 28 weeks to 32 weeks (20 cases), and 32 weeks to 34 weeks (17 cases). The birth weight ranged from 880 to 2460g, with less than 1000g (3 cases), 1000 to 1500g (14 cases), and 1500 to 2500g (23 cases). There were 3 cases in neonatal hyaline membrane disease, 3 cases in pneumonia, 10 cases in mild asphyxia, 2 cases in severe asphyxia, 2 cases in pulmonary hemorrhage, 3 cases were small for gestational age, 1 case in sepsis, 1 case in cytomegalovirus infection, and 13 cases of disease-free preterm infants.

We found that 32 had normal twisting motion, 8 had poor repertoire, and no cramped-synchronized and chaotic were found. NBNA score ≥35 points in 28 cases, <35 points in 12 cases. Cranial MRI imaging revealed 4 cases were extra-cerebral effusion, 2 cases were bilateral frontal softening foci and extra-cerebral effusion. It was found 2 cases delayed myelination, 1 case had a wide septum, 1 case had bilateral ventricular enlargement, and 1 case had a weakened white matter. A total of 11 cases had imaging changes.

The correlation analysis between the 3 methods results GMs quality assessment and NBNA rank correlation coefficient was 0.491 (P = .001), head MRI and NBNA rank correlation coefficient was 0.452 (P = .002), GMs assessment and head MRI rank correlation coefficient was 0.392 (P = .012). There was a correlation between 3 groups. The GMs assessment and the NBNA rank correlation coefficient were higher than the others, as shown in Table 1.

4. Discussion

Preterm birth is a high risk factor resulting in neurodevelopmental abnormalities in infants. According to the study investigating the high-risk influences of children with cerebral palsy, preterm birth is the leading cause and the relative risk of cerebral palsy in infants was 25.16 times higher than full-term infants. Preterm infants with other risk factors are more likely to occur abnormal development of the central nervous system. Early detection and intervention are necessary to reduce the incidence of disability.

GMs assessment is a new neurological approach for early diagnosis of childhood developmental disorders created in 1990 by Heinz Prechtl, the father of Austrian developmental

Table 1

| Methods | GMs | MRI | Total | NBNA | GMs | Total | MRI | NBNA |
|---------|-----|-----|-------|------|-----|-------|-----|------|
| +       | 5   | 3   | 8     | +    | 6   | 12    | +   | 4    |
| −       | 6   | 26  | 32    | −    | 2   | 26    | 28  | −    |
| r       | 0.392 | 0.491 | 0.452 |
| P       | .012 | .001 | .002  |

GMs = general movements, MRI = cerebral magnetic resonance imaging, NBNA = neonatal behavior neurological assessment.
neurology.[11] It is based on Gestalt perception, and previous studies have reported that the rater agreement is 90% (the average Cohen Kappa is 0.88), indicating the objectivity and stability of the method.[12] Multiple studies have shown that GMs can not only predict the neurodevelopmental outcomes of premature babies and infants, especially cerebral palsy, but also predict the cognitive and behavioral impairment of school-age children.[11,13,14] GMs alter complex and variable features if the nervous system is damaged.[15] Through multiple recordings of GMs, different ages of GMs individual development trajectory were obtained, which made an accurate prediction of the individual neurodevelopment outcomes. The breakthrough point lies on the reliable predictions of severe neurodevelopmental disorders at a super-early stage.[16] Zhong et al[17] conducted follow-ups using 58 high-risk newborns. The results showed that for full-term newborns, the predictive validity of GMs assessment at the previous stage for cerebral palsy was 83% for sensitivity, 78% for specificity, 50% for positive predictive value, and 95% for negative predictive value, indicating GMs has good predictive ability for cerebral palsy. NBNA is widely used as a high-risk infants screening method by Chinese Children’s Health Department, which can comprehensively reflect the functional status of the brain, especially the degree of damage to the cerebral cortex.[18] Zhang et al[19] scored 396 high-risk newborns with NBNA, and the score was significantly lower than that of normal newborns. In addition, the traditional cranial MRI is a morphological reflection of the central nervous system. It is reported that in terms of neural imaging examination, the cranial MRI detection reached a positive rate of 70% to 90%, the accuracy was high in predicting long-term brain development disorders, especially cerebral palsy.[20] All the subjects in this study were preterm infants with high-risk in abnormal neurodevelopment. A total of 40 subjects were included in the follow-up. Eight cases were positive for GMs, 12 cases were NBNA scores <35 points, and 11 cases were positive for cranial MRI examination. There was a correlation among the 3 groups (P < .05), the inter-group rank correlation coefficients were 0.491 (GMs and NBNA), >0.452 (MRI and NBNA), and >0.392 (GMs and MRI). The rank correlation coefficient of GMs and NBNA was higher than other groups. Cranial MRI reflects brain structure, while GMs and NBNA reflect brain function. There was an internal correlation between these 3, consistent with the inter-group correlation in this study. In this study, the positive rate of NBNA detection was the highest, with a total of 12 abnormal cases. However, similar to GMs, the requirements of operation on the site and environment were strict. There were 11 abnormal cases in cranial MRI, and studies have shown that the skull imaging structure of preterm infants with partial external hydrocephalus and widened septum pellucidum returned to normal when the follow-up period reached to 12 months of correct gestational age.[21] In addition, some preterm infants without abnormal MRI structures in early stage may have backwardness in neurodevelopment in the future. The study was short in duration and failed to follow up on the final brain development outcomes, but the 3 neurological assessment predicted the nervous system in an early stage and resulted in a good correlation. The theory of brain development suggests that the early brain has plasticity, specifically, the mutability and compensatory. And early intervention will greatly promote brain plasticity and achieve good compensatory.[22] The most important thing is that within 6 months after birth, when the brain is in a period of rapid growth and development, and abnormal postures and movements are not solidified, early detection and intervention can maximally reduce the disability incidence of high-risk infants.[23] In practice, cranial MRI examinations are costly, time-consuming, and not widely used. In addition, sedation is required, with high risk during surgical procedure. GMs do not require special medical equipment in clinical applications, and mainly evaluate the complexity, variability, and flow of early spontaneous movements in infants, which can predict cerebral palsy in preterm infants at an early stage. Moreover, GMs evaluation can be used directly for preterm infants without age correction, which has certain advantages compared with NBNA. In our research, GMs and NBNA have a higher rank correlation coefficient than other groups, and is easy to operate at the small hospitals, therefore it can be more widely used in hospitals. The main limitation of this research was small sample size studied in a single center. In the future, we will further expand the sample size to and extend the research time to make the results stronger and more reliable.

In summary, the GMs assessment is a non-invasive and non-interfering method, which is particularly easy to be accepted by parents. It is suitable for evaluating the brain development of preterm infants, and is expected to become a new tool that is simple, practical, and easy to promote. Furthermore, the GMs assessment in preterm infants is correlated with NBNA and cranial MRI examination. To the best of our knowledge, this is the first time to study the relevance of GMs, NBNA, and MRI. The GMs assessment combined with NBNA assessment of the nervous system development of preterm infants can be carried out and promoted in medical institutions in the future.

Author contributions

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References

[1] Limperopoulos C. Long-term medical and social consequences of preterm birth. N Engl J Med 2008;359:262–73.
[2] Bax M, Tydeman C, Flodmark O. Clinical and MRI correlates of cerebral palsy: the European Cerebral Palsy Study. JAMA 2006;296:1602–8.
[3] Bao XL, Yu RJ, Li ZS. 20-item neonatal behavioral neurological assessment used in predicting prognosis of asphyxiated newborn. Chin Med J 1993;106:211.
[4] Adde L, Helbostad JL, Jensensius AR, Taraldsen G, Grunewaldt KH, Stoen R. Early prediction of cerebral palsy by computer-based video analysis of general movements: a feasibility study. Dev Med Child Neurol 2018;61:277–81.
[5] Adde L, Nygg M, Lossius K, Oberg GK, Stoen R. General movement assessment: predicting cerebral palsy in clinical practise. Early Hum Dev 2007;83:13–8.
[6] Sharp M, Coenen A, Amery N. General movement assessment and motor optimality score in extremely preterm infants. Early Hum Dev 2018;124:38–41.
[7] Jiang M, Zhang Q, Zhang W, et al. Effect of parenting training on neurobehavioral development of infants. Med Sci Monit 2020;26:924457.
[8] Volpe JJ. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. Lancet Neurol 2009;8:110–24.
[9] Blackburn S. Central nervous system vulnerabilities in preterm infants, part II. J Perinat Neonatal Nurs 2009;23:108.

[10] Spittle AJ, Orton J, Doyle LW, Boyd R. Early developmental intervention programs post hospital discharge to prevent motor and cognitive impairments in preterm infants. Cochrane Database Syst Rev 2010;3:209–12.

[11] Hadders-Algra M. Neural substrate and clinical significance of general movements: an update. Dev Med Child Neurol 2017;60:39–46.

[12] Einspieler C, Prechtl HFR. Prechtl’s assessment of general movements: a diagnostic tool for the functional assessment of the young nervous system. Ment Retard Dev Disabil Res Rev 2010;16:61–7.

[13] Xie K, Zheng H, Li H, et al. The study of effect for general movements assessment in the diagnosis of neurological development disorders. Clin Pediatr 2015;55:36–43.

[14] Novak I, Morgan C, Adde L, et al. Early, accurate diagnosis and early intervention in cerebral palsy: advances in diagnosis and treatment. JAMA Pediatr 2017;171:897–907.

[15] Seme-Ciglenecki P. Predictive value of assessment of general movements for neurological development of high-risk preterm infants: comparative study. Croat Med J 2003;44:721–7.

[16] Einspieler C, Prechtl HFR, Ferrari F, Cioni G, Bos AF. The qualitative assessment of general movements in preterm, term and young infants: review of the methodology. Early Hum Dev 1997;50:47–60.

[17] Zhong C, Yang H, Wang WX, Zhou LF, Zhang XL. Comparison of predictive validity of two assessment methods for gross motor outcome and cerebral palsy in high risk infants. Chin J Child Health Care 2015;23:856–8.

[18] He G, Wu J, Luo W. Research on early intervention to high risk infant by taking 20 items of neonatal behavioral neurological assessment. Hebei Med 2003;9:97–9.

[19] Zhang XY, Hong-Ru LU, Song HX, Liu L. Assessment of brain development and brain injury of preterm infants by neonatal behavioral neurological assessment. Chin J Child Health Care 2010;18:159–62.

[20] Rijn AMR, Groenendaal F, Beek FJA, Eken P, Haastert ICV, Vries LSD. Parenchymal brain injury in the preterm infant: comparison of cranial ultrasound, MRI and neurodevelopmental outcome. Neuropediatrics 2001;32:80.

[21] Spittle AJ, Boyd RN, Inder TE, Doyle LW. Predicting motor development in very preterm infants at 12 months’ corrected age: the role of qualitative magnetic resonance imaging and general movements assessments. Pediatrics 2009;123:512.

[22] Alvaradoguerrero I, Poblano A, Marosi E, Corsicabrera M, Oteroojeda GA. Early intervention in the neurodevelopment of premature infants during the first six months of life. Neurosci Med 2011;2:104–9.

[23] Chen GF, Zhang YF, Chen MQ, et al. Early multi-disciplinary intervention reduces neurological disability in premature infants. Chin J Contemp Pediatr 2014;16:35–9.