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Correlation of twisting motion phase and infantile spasms in high risk infants

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Summary

Objective: The aim of this study was to investigate the correlation of twisting motion phase and infantile spasms in high risk infants. *Materials and Methods:* One hundred seventy-eight high-risk newborns experiencing follow-up in the rehabilitation phase were selected and full-body motion quality assessment was performed in the twisting motion phase. The occurrence of infants with infantile spasms after 12 months (corrected age) was statistically analyzed. *Results:* No clear correlation was found between monotonous movement twisting motion phase and infantile spasms, and spasm synchronized movement had no definite prediction for infantile spasms. The incidence of infant spasm with movement form having spastic synchronized characteristics had significant difference compared with monotonous systemic movement ($p < 0.01$). The sensitivity of predictive rate for spasm-synchronous movement of infantile spasms was 90.9%, the specificity was 96.8%, the positive predictive value was 80%, and the negative predictive value was 98.7%. *Conclusions:* Spasm synchronized movement had some predictive value for infantile spasms in twisting motion stage. The newborns with this kind of movement form should be checked by regularly ambulatory EEG.

Key words: General movements; Twisting motion; Infantile spasms; Risk newborns.

Introduction

Infantile spasms is a special epilepsy, also known as West syndrome, which was firstly described in detail by British doctors West in 1841 with three characteristics (nod seizures, progressive mental regression, and high-degree imperfect EEG) [1]. The disease is the most common form of age-dependent epileptic encephalopathy with characteristics such as difficult to be treated and poor prognosis. Mental development retardation is often found in the follow-up of infants with infantile spasms, and many merged infantile spasms also existed in infants with cerebral palsy or mental retardation. The average incidence of the disease is about 0.31% [2]. The studies of Rantala *et al.* [3] showed that the incidence increased significantly in the high-risk newborns. The so-called high-risk newborns are infants who are prone to perinatal brain damage, cerebral palsy, mental retardation, epilepsy, and other diseases, including premature birth, low birth weight, perinatal asphyxia, fetal distress, sustained hypoxia, cranial hemorrhage, severe hypoglycemia, severe hyperbilirubinemia and other risk factors [4, 5]. The possibility of different brain developmental factors combined infantile spasms is not the same. This occurrence of spasm was often not distinguished from other normal or abnormal behavior of infants acts, abnormality of the nervous system is detected in about 2/3 of the affected infants [6]. This makes it more difficult to diagnose the infantile spasms. Although mental retardation occurs in almost all of the infants whose infantile spasms cannot be effectively controlled by drug, but this is the development qualification for the development of infantile spasms, rather than the performance of infantile spasms. However, the incidence of infantile spasms may further cause brain damage and mental damage [7]. Abnormalities (structural or functional) of the nervous system is likely to be the root causes of infantile spasms. No proper and timely treatment is given for infantile spasms and will often cause disastrous consequences [8]. How to timely discover infantile spasms and give appropriate treatment have a very significantly prognostic significance.

The latest research showed that quality assessment technology of general movements (GMs) is more sensitive and reliable as a new method for predicting early assessment of brain injury compared with the traditional neurological examination and imaging, especially having special predictive value for cerebral palsy [9, 10]. As a common complication of infants with cerebral palsy, epilepsy is known to have close relation with cerebral palsy. The researches by the domestic institutions on the correlation between general movement quality assessment as the earliest and most sensitive technology and infantile spasms (the particular form of epilepsy) has not yet been statistically analyzed. This project was carried out in the present hospital since 2009 and it was found that the infantile spasms occurred in different abnormal movement patterns in the twisting movement phase in the general movements, but the incidence was different.

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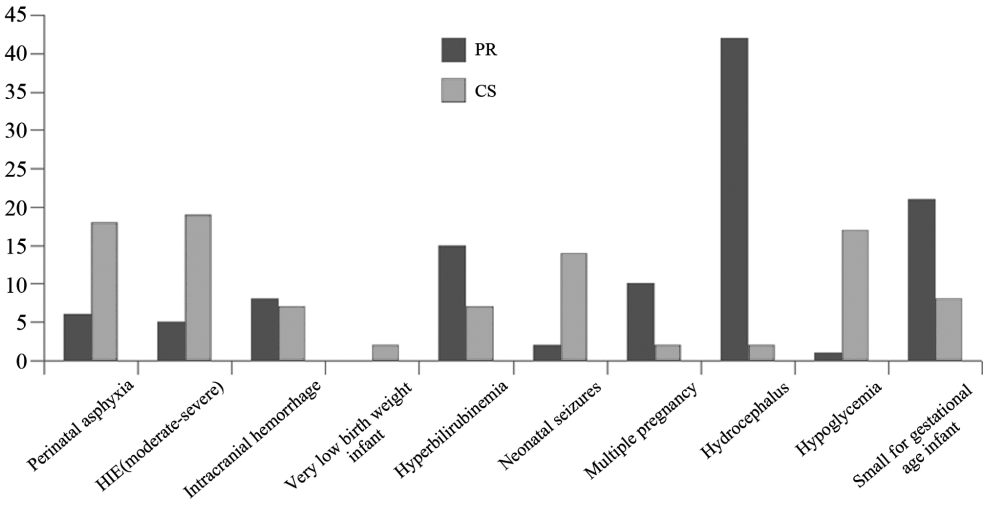

Figure 1. — Distribution of major risk factor abnormal movement patterns in twisting motion stage.

In order to identify the correlation between twisting movement phase and infantile spasms, the study was performed as follows.

Materials and Methods

Experimental objects

Two hundred and one high-risk newborns experiencing neurodevelopmental follow-up during April, 2011 and April, 2012 in rehabilitation department of Xuzhou Children's Hospital were selected; the follow-up time was more than one year. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Soochow University. Written informed consent was obtained from all participants.

Inclusion criteria: 1) GMs were recorded for at least once in twisting motion stage and 2) a clear follow-up outcome. Exclusion criteria: 1) no clear pre-production period, 2) diagnosed to be a genetic metabolic disease, 3) infantile spasms were not diagnosed in the present hospital, 4) infants lost to follow-up. A total of 178 cases were selected to be study objects with males in 112 cases and females in 66 cases, including preterm children in 98 cases (74 males and 24 females), gestational age of 28-36 weeks with mean of 32.8 ± 2.6 weeks, birth weight of 1,100 - 3,150 grams with average of 1,960 ± 566 grams.

GMs assessment

In four weeks corrected gestational age, video-recording was used to document the standardized GMs of the research subjects, with ten to 15 minutes given for each record. All video data were jointly evaluated by three evaluators. Evaluators have assessed experience of more than one year and obtained qualification certificates by participated in the training of GMs Trust. The consistency of the assessment results from three evaluators was 95%. Inconsistent assessment results were further decided by discussions and consultations of the three evaluators. Three evaluators were unaware of the basic data of the research objects.

Assessment results record

Twisting motion stage: normal GMs were recorded as N. Abnormal GMs were recorded as three subtypes including PR (monotonic), CS (spasm-synchronization) and CH (confusion). Several evaluators took the results of the last assess GMs as the statistical materials.

Infantile spasms

Diagnosis of spasm: infantile spasms were diagnosed by neurologist in the present hospital, the diagnostic criteria included that the seizures occurred within one year of age or rarely for more than two years of age, highly imperfect EEG characteristics, often clusters of the clinical seizures, also appearing alone, and often accompanied by developmental stagnation or retrogression [11].

EEG

EEG examinations were also carried in the present hospital. The infants with abnormalities in twisting motion stage were commonly performed routine EEG, and ambulatory EEG monitoring was further performed to the newborns with abnormalities in regular EEG. Reviewed once every 45 days if the seizures were not clear and reviewed at any time if the similar seizures occurred.

Predictive validity

Predictive validity indicators included prediction sensitivity (positive proportion in the diagnostic tests for the ill persons determined by the gold standard for the diagnosis), prediction specificity (negative proportion in the diagnostic tests for the persons without illness determined by the gold standard for the diagnosis), positive predictive value (ill person proportion by the gold standard for the diagnosis in the positive diagnostic tests), negative predictive value (without ill person proportion by the gold standard for the diagnosis in the negative diagnostic tests). Statistical analysis was performed using the SPSS statistical software.

Results

A total of 178 cases study objects (male in 112 cases and female in 66 cases) were collected. The corrected gestational age was within four weeks. Eighty-three cases were recorded to be normal in GMs assessment without occurrence of infantile spasms. Ninety-five cases were abnormal, including 22 cases had the occurrence of infantile spasms (23.2%) and 73 cases without infantile spasms (76.8%). Tables 1 and 2 indicate that the positive predictive of infantile

Table 1. — *Predictive validity of CS in infantile spasms.*

GMs	Infantile spasms	Without infantile spasms	Total
CS	20	5	25
PR+N	2	151	153

Table 2. — *Different types of abnormal twisting motion and infantile spasms*

GMs	Infantile spasms	Without infantile spasms	Total
PR	2	68	70
CS	20	5	25

Note: The incidence of infantile spasms in the two groups was analyzed by chi-square test ($p < 0.01$). χ^2=61.6, degrees of freedom was 1 and the difference was statistically significant.

Table 3. — *Predictive validity of abnormal twisting motion in infantile spasms (cases).*

GMs	Infantile spasms	Without infantile spasms	Total
PR+CS	22	73	95
N	0	83	83

spasms by general body motion abnormalities (PR and CS) was low (23.2%). Many high-risk newborns did not have infantile spasms. The positive predictive value of CS movement mode in the twisting motion stage for infantile spasms significantly increased (80%), indicating that the possibility of high-risk newborns with performance of early CS having infantile spasms was great. The incidence of infantile spasms with PR and CS performance showed statistically significant differences.

The distribution of the major risk factors for abnormal movement patterns in twisting motion phase is shown in (Figure 1). The primary factors in the history of spastic infants with synchronous movement characteristics were perinatal asphyxia, severe hypoxic-ischemic encephalopathy (HIE), neonatal seizures, and low blood sugar, suggesting severe brain injury may be the reasons for spastic synchronous general movement.

The predictive sensitivity of abnormal twisting motion for infantile spasms was 100%, the predictive specificity was 53.2%, the positive predictive value was 23.2%, and the negative predictive value was 100% (Table 3).

Predictive sensitivity was 90.9% and specificity was 96.8%, the positive predictive value was 80%, while the negative predictive value was 98.7% (Table 1).

The incidence of infantile spasms groups was analyzed by chi-square test ($p < 0.01$, $\chi^2 = 61.6$, degrees of freedom was 1) and the difference was statistically significant (Table 2).

Discussion

Cerebral palsy is one of the major diseases causing disability in children. Patients with cerebral palsy could be seen in all types of seizures. Epilepsy was often associated with cerebral palsy in newborns with high incidence, difficult diagnosis, and poor prognosis [12]. Epilepsy combined cerebral palsy was often difficult to control and easily transferred into intractable epilepsy and epilepticus status, which needed two or more kinds of antiepileptic drugs to treat. The epileptic seizures of these newborns will cause further damage of the existing movement, speech, and cognitive abilities, thereby rehabilitation efficacy might be damaged because of epileptic seizures. West syndrome was a severe epileptic encephalopathy of infancy with a poor developmental outcome [13]. The mortality rate was 5% to 30%; only 7.7%-16% of the normal intelligence and motor development could be restored in the survival infants, and 34.5%-68% of disease newborns had severe mental retardation and motor defects. The Primec *et al.* study [14] pointed out that if treatment started within a month of the spasm seizures, the seizures would be well-controlled and the development would be improved. For the newborns with low age with abnormal movement patterns, the diagnosis of epilepsy was particularly difficult and the seizures were different between infants and adults [15].

West syndrome or infantile spasms is one of the most frequent epileptic syndromes in the first year of life. The clinical symptoms of infantile spasms are very different from any other type of seizure because of both the absence of paroxysmal motor phenomena (i.e., as in a convulsion) and the lack of significant duration of loss of consciousness (i.e., as in absence epilepsy). The performance of newborn seizures might be mistaken for new parents abnormal movement patterns or muscle tension due to unclear delivery to the doctor, or newborn seizures cannot be found because of their short duration, thus epilepsy would be further aggravated. The movement intelligence, verbal, cognitive and other aspects of the infants is further damaged. The Auvin *et al.* study [16] also indicated that a poor outcome was related to a delay in diagnosis, which was observed regardless of the existence of cognitive involvement prior to the start of infantile spasms (relative risk: RR 12.08 [1.52 - 96.3]). These results highlighted the importance of making an early diagnosis of infantile spasms. How to perform early detection, diagnosis, and effective treatment is the top priority in the rehabilitation programs for children.

General movement quality assessment was first proposed by Austrian development neurologist Einspieler *et al.* in 1990 [17], which has been used as an effective tool to assess neurodevelopmental outcomes. Currently, GMs quality assessment has been widely used in foreign clinical follow-up among high-risk neonatal neurological development [18]. If the spasm synchronous systemic movement patterns continuously exist in a few weeks, they often show lack of restless movement in the development into restless movement stage, which has higher predictive value for the developmental outcomes of spastic cerebral palsy [19].

In the present study, there were 22 cases with infantile spasms (23.2%) and 73 cases without infantile spasms (76.8%) in the newborns with general motion abnormalities. The positive predictive value of general motion abnormalities in the twisting stage (PR and CS) was low (23.2%). Twenty cases with infantile spasms in the twisting motion stage had CS, accounting for 90.9%. The positive predictive value of CS movement mode for infantile spasms increased significantly (80%). The incidence of newborns with infantile spasms performing PR and CS were significantly different by statistical analysis, suggesting that the synchronization of general movement and spastic infantile spasms had a very high correlation with some predictive value, which was highly correlated between continued CS movement patterns and spastic cerebral palsy, while spastic quadriplegia and age-dependent epileptic encephalopathy had a good correlation. This study was consistent with the study results of Sugiura *et al.* [20].

The studies of Hrachovy and Frost [2] showed that spasms usually occurred during drowsiness or arousal from sleep and the average age was six months. In the 22 cases with infantile spasms in the present study, the youngest with onset was two months and the oldest was ten months with a mean of 5.86 months, which was consistent with the study of Hrachovy and Frost.

The present study also found that the primary factor accounting for the history of newborns with spastic synchronous movement characteristics were perinatal asphyxia, severe HIE, neonatal seizures, and low blood sugar, suggesting that severe brain injury may the reasons for infants with spastic synchrony general movement and the poor effect of combined infantile spasms and anti-epileptic treatment [21]. This study was consistent with the study results of Gano *et al.* [21].

The diagnosis and treatment for infantile spasms combined with cerebral palsy were the most difficult. In diagnosis, attention should be paid to the difference with spastic synchronization general movement mode, in which the latter includes no seizures, some performances at the time of seizure such as abnormal eye movements and autonomic nerve phenomena generally did not appear in the above-mentioned types of body movement. Dynamic EEG was still indispensable in diagnosis of infantile spasms. In treatment, difficult problem was the necessity of combining the principles of antiepileptic treatment with movement disorders recovery. Epilepsy often resulted in suspension and increased dyskinesia rehabilitation. After the diagnosis of epilepsy in infants with cerebral palsy, the rehabilitation measures have to be arrested and the rehabilitation programme should be adjusted. The drug control of seizures should be the first step in a new rehabilitation program.

It should be noted that for the clear diagnosis of infantile spasms, long-term follow-up was necessary after markedly efficacy in the initial treatment. Relapse was common and the transfer into other forms of epilepsy was also seen clinically after one or two years of age [22]. In addition, newborns with spastic synchronous movement patterns may be associated with metabolic disorders at a certain degree. The anti-epileptic treatment of the consolidation of infantile spasms in these infants also required liver and kidney function assessments. As for the infants with CS motion feature but not yet infantile spasms, doctors should pay attention to reasonable and appropriate use of nerve cell nutrients in the early intervention rehabilitation and inform the possibility of merging infantile spasms and onset performance to the parents of the newborns. Regular ambulatory EEG monitoring should be performed for timely detection and treatment when infantile spasms occur in order to minimize brain damage.

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References

[1] Wray C.D., Benke T.A.: "Effect of price increase of adrenocorticotropic hormone on treatment practices of infantile spasms". *Pediatr. Neurol*., 2010, *43*, 163.
[2] Hrachovy R.A., Frost J.D. Jr.: "Infantile spasms". *Handb. Clin. Neurol*., 2013, *111*, 611.
[3] Rantala H., Shields W.D., Christenson P.D., Nielsen C., Buch D., Jacobsen V., *et al.*: "Risk factors of infantile spasms compared with other seizures in children under 2 years of age". *Epilepsia*, 1996, *37*, 362.
[4] Guralnick M.J., Bennett F.C.: "The effectiveness of early intervention for at-risk and handicapped children". New York: Academic Press Inc Harcourt Brace Jovanovich Publishers, 1991, 79.
[5] Collin M.F., Halsey C.L., Anderson C.L.: "Emerging developmental sequelae in the 'normal' extremely low birth weight infant". *Pediatrics*, 1991, *88*, 115.
[6] Hancock E.C., Osborne J.P., Edwards S.W.: "Treatment of infantile spasms". *Cochrane Database Syst. Rev.*, 2013, *6*, CD001770.
[7] Fejerman N.: "Differential diagnoses of West syndrome". *Rev. Neurol*., 2013, *57*, S125.
[8] Yu J.Y., Pearl P.L.: "Metabolic causes of epileptic encephalopathy". *Epilepsy Res. Treat*., 2013, *2013*, 124934.
[9] Einspieler C., Prechtl H.F.: "Prechtl's assessment of general movements: a diagnostic tool for the functional assessment of the young nervous system". *Ment. Retard. Dev. Disabil. Res. Rev*., 2005, *11*, 61.
[10] Prechtl H.F.: "General movement assessment as a method of developmental neurology: new paradigms and their consequences". *Dev. Med. Child. Neurol.*, 2001, *43*, 836.
[11] Pavone P., Striano P., Falsaperla R., Pavone L., Ruggieri M.: "Infantile spasms syndrome, West syndrome and related phenotypes: What we know in 2013". *Brain Dev*., 2013.
[12] Kułak W., Sobaniec W.: "Risk factors and prognosis of epilepsy in children with cerebral palsy in north eastern Poland". *Brain Dev*., 2003, *25*, 499.
[13] Japaridze N., Muthuraman M., Moeller F., Boor R., Anwar A.R., Deuschl G., *et al.*: "Neuronal networks in west syndrome as revealed by source analysis and renormalized partial directed coherence". *Brain Topogr*., 2013, *26*, 157.
[14] Primec Z.R., Stare J., Neubauer D.: "The risk of lower mental outcome in infantile spasms increased after thee weeks of hypsarrhytmia duration". *Epilepsia*, 2006, *47*, 2202.

[15] Yu H.J., Lee C.G., Nam S.H., Lee J., Lee M.: "Clinical and ictal characteristics of infantile seizures: EEG correlation via long-term video EEG monitoring". *Brain Dev.*, 2013, *35*, 771.
[16] Auvin S., Hartman A.L., Desnous B., Moreau A.C., Alberti C., Delanoe C., *et al.*: "Diagnosis delay in West syndrome: misdiagnosis and consequences". *Eur. J. Pediatr.*, 2012, *171*, 1695.
[17] Einspieler C., Prechtl H.F., Ferrari F., Cioni G., Bos A.F.: "The qualitative assessment of general movements in preterm, term and young infants-review of the methodology". *Early Hum. Dev*., 1997, *50*, 47.
[18] Hadders-Algra M.: "General movements: a window for early identification of children at high risk for developmental disorders". *J. Pediatr*., 2004, *145*, S12.
[19] Yang H., Einspieler C., Shi W., Marschik P.B., Wang Y., Cao Y., *et al.*: "Cerebral palsy in children: Movements and postures during early infancy,dependent on preterm vs. full term birth". *Early Hum. Dev*., 2012, *88*, 837.
[20] Sugiura C., Shiota M., Ieshima A., Ohno K.: "Epilepsy in patients with cerebral palsy-analysis of frequency and clinical prognosis". *No To Hattatsu*, 2003, *35*, 478.
[21] Gano D., Sargent M.A., Miller S.P., Connolly M.B., Wong P., Glass H.C., *et al.*: "MRI findings in infants with infantile spasms after neonatal hypoxic-ischemic encephalopathy". *Pediatr. Neurol*., 2013, *49*, 401.
[22] Sanmaneechai O., Sogawa Y., Silver W., Ballaban-Gil K., Moshé S.L., Shinnar S.: "Treatment outcomes of West syndrome in infants with Down syndrome". *Pediatr. Neurol*., 2013, *48*, 42.

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