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The Study of Effect for General Movements Assessment in the Diagnosis of Neurological Development Disorders: A Meta-Analysis

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Abstract

Objective: To discuss the value of general movements assessment in predicting the neurological disorders. **Methods:** Using PubMed as the search engine, we searched to identify relevant studies in English and Chinese language published up to November 2014 and 19 studies were selected. Standard methods in meta-analyses were used to provide diagnostic accuracy by Meta-DiSc 1.4. **Results:** For non–cerebral palsy (non-CP) as outcome for writhing period, the results suggested a good sensitivity and a specificity of 0.74, the Q-value was 0.80. The area under the curve (AUC) was 0.87. For non-CP as outcome for fidgety period, the results suggested both high level for sensitivity and specificity. And the Q-value was 0.914, the AUC was 0.9664. For CP as outcome for writhing and fidgety periods, good sensitivity and specificity were found in the analysis, and the Q-value was 0.9034 while the AUC was 0.9592. **Conclusion:** General movements assessment is a good predictor for diagnosing neurological disorders.

Keywords

general movements, neurodevelopment, cerebral palsy, meta-analysis

Introduction

General movements (GMs) are complex movements that arise from early fetal life and persist until 3 to 4 months, involve movements of head, trunk, arms, and legs. During the past few years, it has become clear that the quality of GMs of young infants is a powerful predictor of the development of neurological disorders, including cerebral palsy (CP).[1,2] Normal GMs are characterized by fluency, variation, and complexity and the form changes with increasing of the age. Two forms of abnormal GMs include (*a*) mildly abnormal GMs with lack of fluent movement but still showing some complexity of movements and variation and (*b*) definitely abnormal GMs, which show the lack of movement fluency, variation, and complexity altogether. The persistent presence of definitely abnormal GMs during the 3 (in preterm infants) or 2 (in term infants) GMs phases put an infant at high risk for the development of a neurological disability. Also, the presence of definitely abnormal GMs at fidgety-GM age, implying the total absence of normal fidgety "dance," indicates a high risk for the development of CP.[3-5]

The qualitative differences in general movements are expressed during 2 periods. In the initial writhing period, from birth at term to 8 weeks postterm, the movements are usually slow, powerful, and elliptical and are generally expressed with variable speed and amplitude and performed close to the body. The overall form is one of fluency and elegance. The second period starts from 6 to 8 weeks until 15 to 20 weeks postterm, the quality of the GMs takes on a new form and the movements are called fidgety movements. In this period, the movements present as small, rounded, continuous movements of the head, trunk, and limbs with small amplitude and moderate speed and variability in direction.[6,7]

Assessment of the quality of GMs in early infancy is a powerful instrument for prediction. The aim of the

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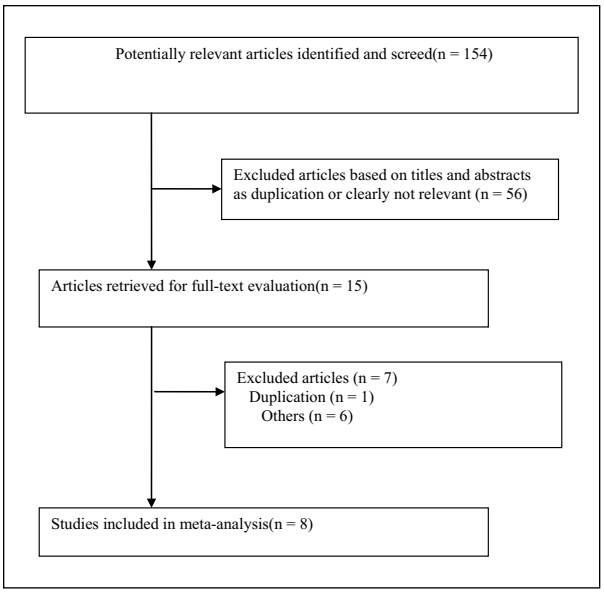

Figure 1. Flowchart of studies identified, included, and excluded.

present study is to discuss the value of GMs evaluation in predicting the disorders of neurological development.

Materials and Methods

Identification of Studies

The databases Medline (using PubMed as the search engine), Embase, Ovid, Web of Science, Cochrane database, and China Journal Net and other databases were searched to identify relevant studies published up to November 2014. No lower date limit was applied. Relevant references of articles were also searched manually. The studies were identified using the following keywords: "general movements," "neurological development," "sensitivity," "specificity," and "accuracy." The language of publication was limited to English and Chinese. Letters to journal editors and conference abstracts, however, were excluded due to limited data. Two authors independently identified eligible studies when screening the searched studies. Any disagreements were arbitrated by a third author.

Quality Assessment

To assess the methodology of the included studies,[4-14] the present meta-analysis was conducted in line with the Quality Assessment for Studies of Diagnostic Accuracy Statement (QUADAS). And evaluation was conducted by 2 authors independently. A third author arbitrated any disagreements. All the data were extracted by 2 of the authors, who were blinded to publication details, such as author details, journal, patient characteristics, test method, cutoff value, sensitivity, specificity, and methodological quality. When multiple publications of the same study were identified, data were extracted as a single study.

Statistical Analysis

Standard methods in meta-analyses were used to provide diagnostic accuracy. Then, sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) for each study were calculated. The sensitivity and specificity of each single test threshold identified for each study were used to plot a summary receiver operating characteristic (SROC) curve. Spearman's rank correlation was performed as a test for threshold effect. The χ^2 and Fisher's exact tests were used to detect statistically significant heterogeneity across the studies. The average sensitivity, specificity and other measurements of the studies were calculated. Meta-DiSc 1.4 was used to perform the analysis.

Results

Description of Included Studies

Following the literature search, a total of 154 articles regarding GMs and disorders of neurological development were considered to be eligible for the present meta-analysis. Of these publications, ultimately 19 studies (11 articles) were selected. A flowchart showing the selection of references for meta-analysis is shown in Figure 1.

Quality of Included Studies

In present meta-analysis, there were 13 studies with QUADAS scores ≥10 (Table 1), $P \geq .05$ indicates values that did not reach statistical significance and these factors did not affect diagnostic accuracy. The clinical characteristics and other information are also outlined in Table 1.

Results

Non–Cerebral Palsy as Outcome for Writhing Period

The forest plots of sensitivity and specificity of GMs in the various studies for the diagnosis of writhing period disorders of neurological development are shown in Figure 2. The sensitivity varied between 0.69 and 0.99

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Table 1. Characteristics of the Included Studies.

Study	Year	Period and Outcome	Country	QUADAS
Hadders-Algra and Groothuis,[10] 1999–1	1999	Writhing CP	Netherlands	12
Hadders-Algra and Groothuis,[10] 1999–2	1999	Fidgety CP	Netherlands	12
Groen et al,[7] 2005–1	2005	Writhing neurological development outcome	Netherlands	11
Groen et al,[7] 2005–2	2005	Fidgety neurological development outcome	Netherlands	11
Groen et al,[7] 2005–3	2005	Writhing neurological development outcome	Netherlands	11
Groen et al,[7] 2005–4	2005	Fidgety neurological development outcome	Netherlands	9
Seme-Ciglenecki,[8] 2007	2007	Fidgety neurological development outcome	Slovenia	9
Yuge et al,[6] 2011	2011	Fidgety neurological development outcome	Japan	11
Hamer et al,[4] 2011	2011	Fidgety CP	Netherlands	8
Brogna et al,[2] 2013–1	2013	Writhing CP	Italy	10
Brogna et al,[2] 2013–2	2013	Fidgety CP	Italy	10
Burger et al,[5] 2011–1	2011	Fidgety neurological development outcome	South Africa	9
Burger et al,[5] 2011–2	2011	Fidgety neurological development outcome	South Africa	9
Su et al,[13] 2014	2014	Fidgety CP	China	12
Shi et al,[11] 2011–1	2011	Writhing neurological development outcome	China	11
Shi et al,[11] 2011–2	2011	Fidgety neurological development outcome	China	11
Yang et al,[12] 2007–1	2007	Writhing neurological development outcome	China	10
Yang et al,[12] 2007–2	2007	Fidgety neurological development outcome	China	10
Bao et al,[14] 2014	2014	Writhing neurological development outcome	China	8

Abbreviations: CP, cerebral palsy; QUADAS, Quality Assessment for Studies of Diagnostic Accuracy Statement.

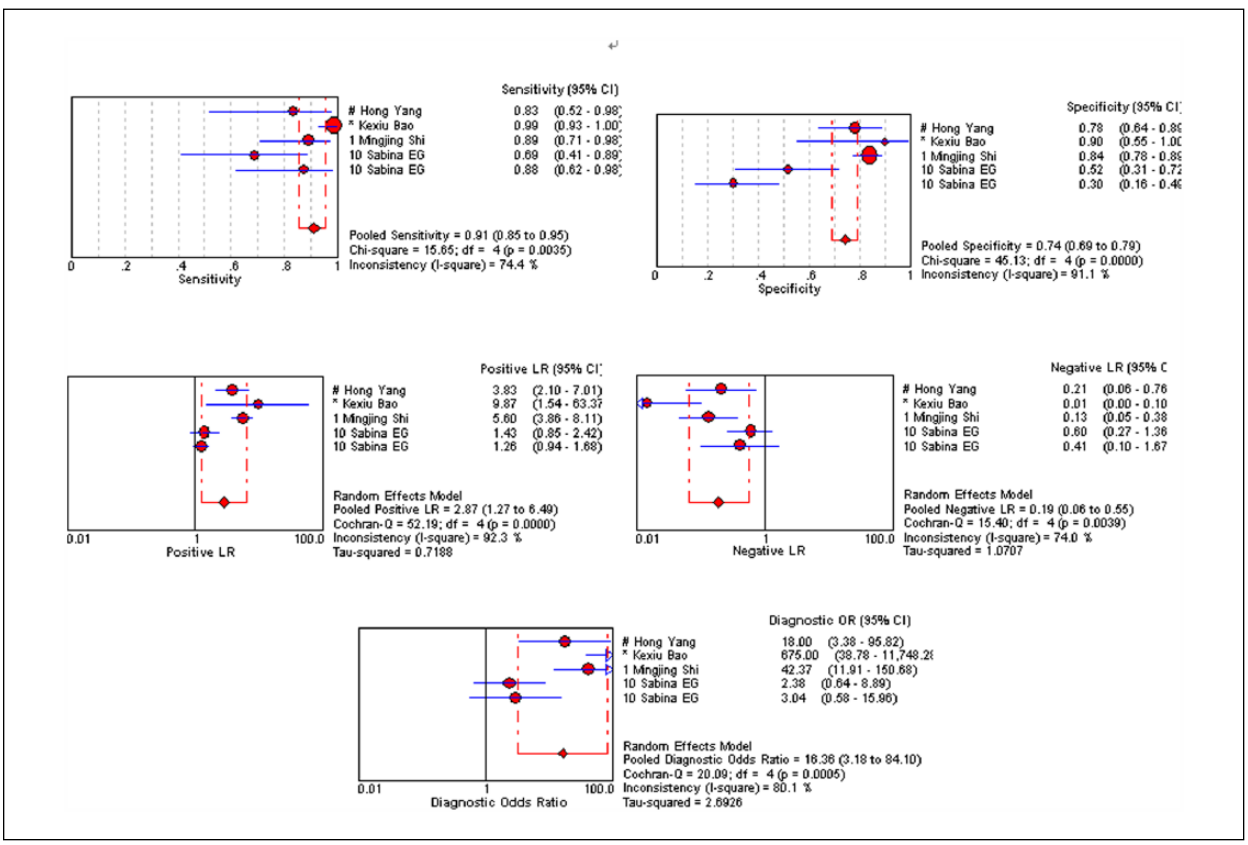

Figure 2. Forest plots of sensitivity and specificity for general movements (GMs) in the diagnosis of writhing disorders of neurological development. The point estimates of sensitivity and specificity from each study are shown as solid circles. Error bars indicate 95% confidence intervals (CIs).

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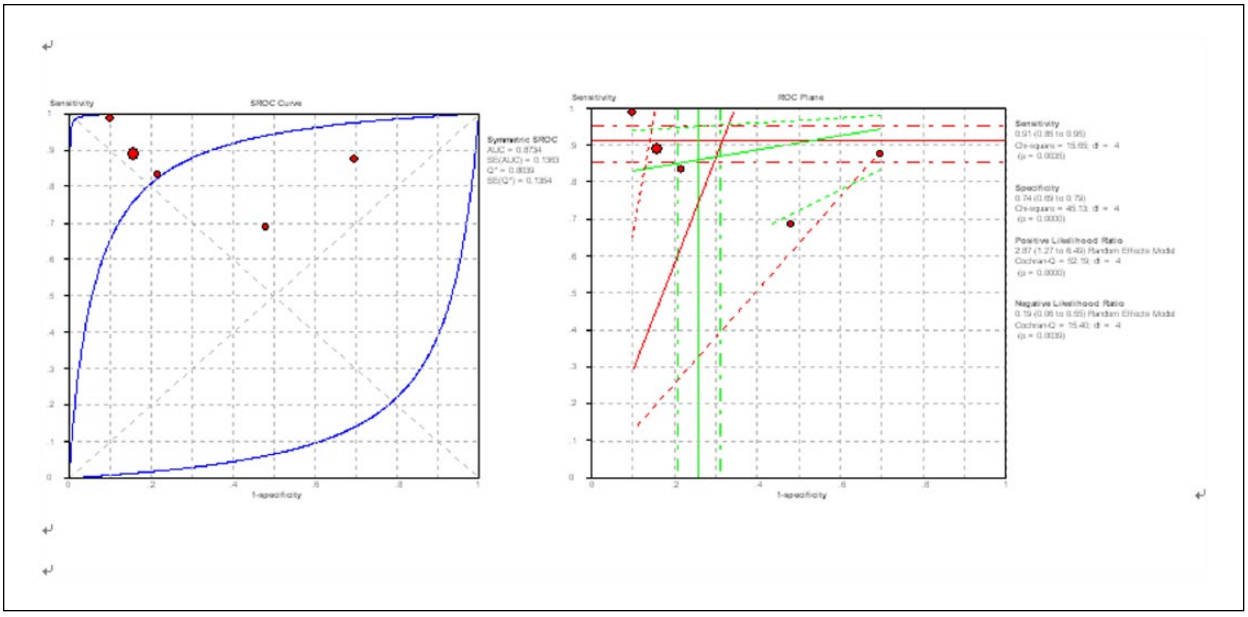

Figure 3. Summary receiver operating characteristic (SROC) curve of general movements (GMs) in the diagnosis of writhing disorders of neurological development. The size of each solid circle represents the sample size of each study. The regression SROC curve indicates the overall diagnostic.

(pooled 0.91; 95% confidence interval [CI], 0.85-0.95), while the specificity ranged from 0.30 to 0.90 (pooled 0.74; 95% CI, 0.69-0.79). The PLR was 2.87 (95% CI, 1.26-6.49), the NLR was 0.19 (95% CI, 0.06-0.76), and the DOR was 16.36 (95% CI, 3.18-84.10). χ^2 values of sensitivity, specificity, PLR, NLR, and DOR were 15.65, 45.13, 52.19, 15.40, and 20.09, respectively, with all *P* values <.001, indicating significant heterogeneity between all studies. The Figure 3 shows the SROC curve, which summarizes the test performance, and shows the balance between sensitivity and specificity. In the present meta-analysis, the maximum joint sensitivity and specificity (the Q-value) was 0.80. The area under the curve (AUC) was 0.87.

Non–Cerebral Palsy as Outcome for Fidgety Period

The forest plots of sensitivity and specificity of GMs in the various studies for the diagnosis of fidgety period disorders of neurological development are shown in Figure 4. The sensitivity varied between 0.75 and 1.00 (pooled 0.98; 95% CI, 0.96-0.98), while the specificity ranged from 0.09 to 0.98 (pooled 0.87; 95% CI, 0.83-0.90). The PLR was 6.97 (95% CI, 0.76-63.66), the NLR was 0.07 (95% CI, 0.02-0.23), and the DOR was 122.79 (95% CI, 23.78-633.97). χ^2 values of sensitivity, specificity, PLR, NLR, and DOR were 75.59, 160.21, 709.83, 40.92, and 36.84, respectively, with all *P* values <.001, indicating significant heterogeneity between all studies. Figure 5 shows the SROC curve, which summarizes the test performance, and shows the balance between sensitivity and specificity. In the present meta-analysis, the maximum joint sensitivity and specificity (the Q-value) was 0.914. The AUC was 0.9664.

Cerebral Palsy as Outcome for Writhing and Fidgety Periods

The forest plots of sensitivity and specificity of GMs in the various studies for the diagnosis of writhing period disorders of neurological development are shown in Figure 6. The sensitivity varied between 0.09 and 1.00 (pooled 0.93, 95% CI, 0.91-0.95), while the specificity ranged from 0.54 to 1.00 (pooled 0.90; 95% CI, 0.86-0.93). The PLR was 5.99 (95% CI, 2.70-13.30), the NLR was 0.08 (95% CI, 0.00-4.95), and the DOR was 88.56 (95% CI, 7.27-1078.85). χ^2 values of sensitivity, specificity, PLR, NLR, and DOR were 214.06, 33.11, 26.80, 437.51, and 34.45, respectively, with all *P* values <.001, indicating significant heterogeneity between all studies. Figure 7 shows the SROC curve, which summarizes the test performance, and shows the balance between sensitivity and specificity. In the present meta-analysis, the maximum joint sensitivity and specificity (the Q-value) was 0.9034. The AUC was 0.9592.

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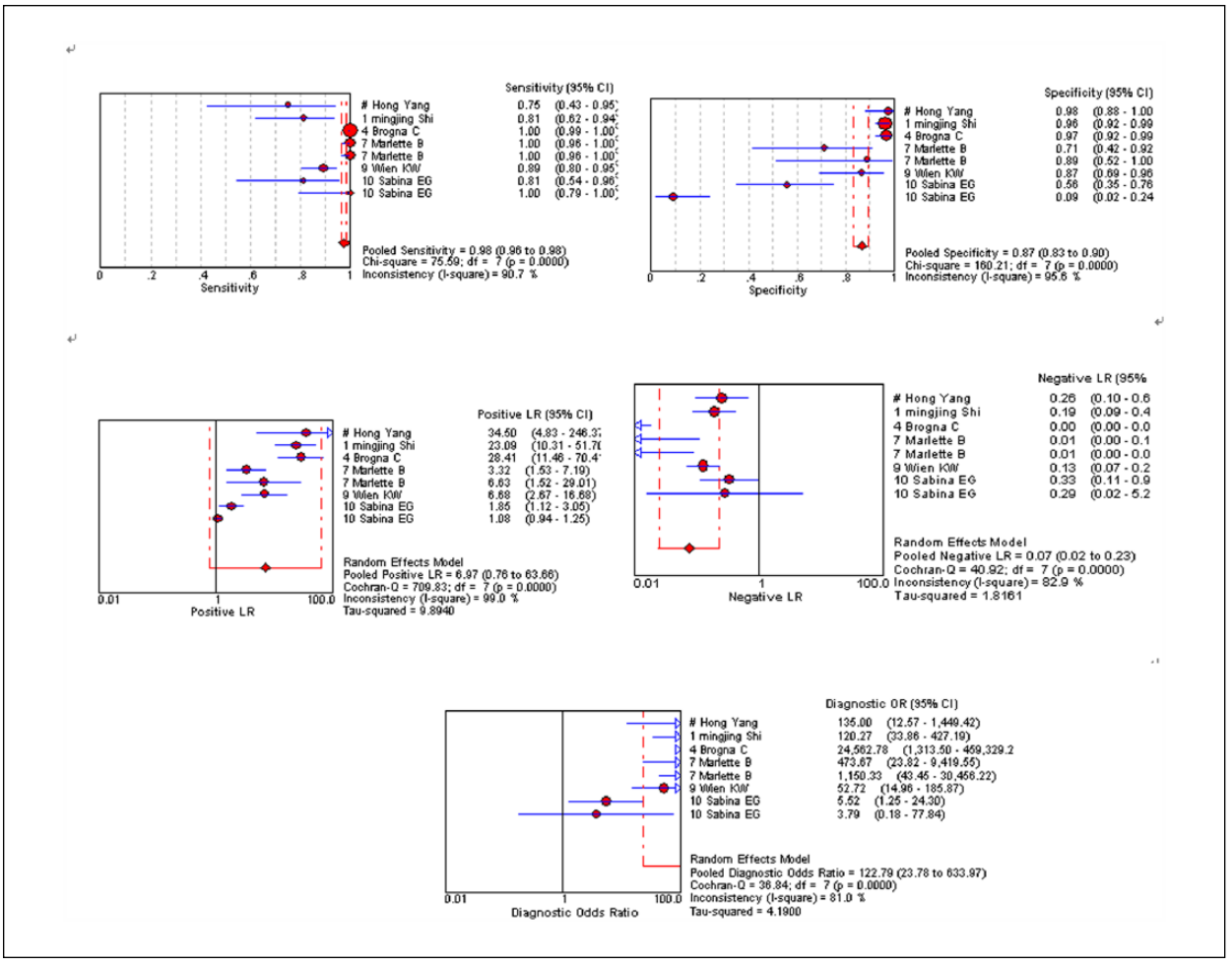

Figure 4. Forest plots of sensitivity and specificity for general movements (GMs) in the diagnosis of fidgety disorders of neurological development. The point estimates of sensitivity and specificity from each study are shown as solid circles. Error bars indicate 95% confidence intervals (CIs).

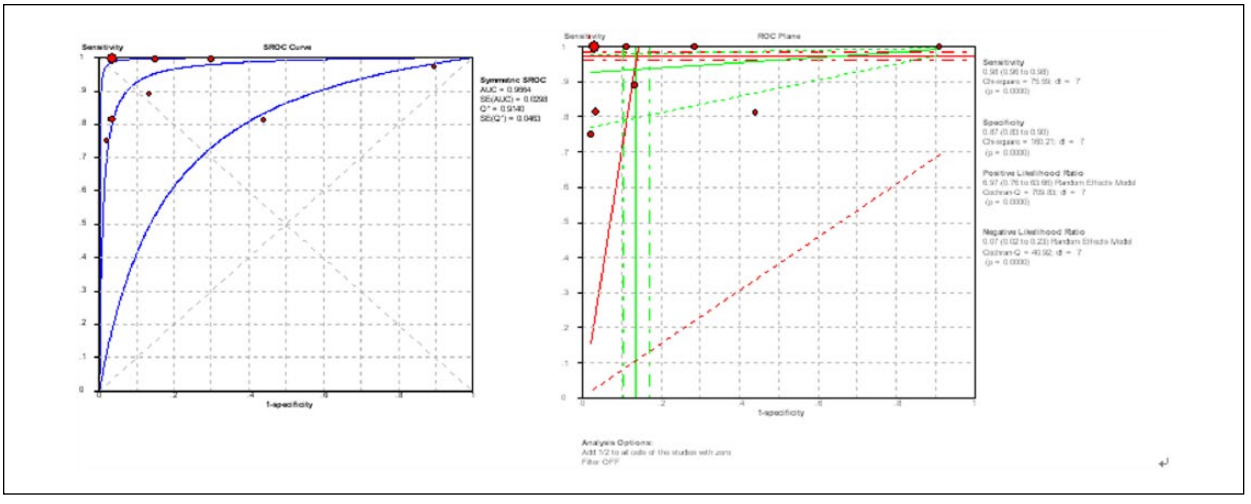

Figure 5. Summary receiver operating characteristic (SROC) curve of general movements (GMs) in the diagnosis of fidgety disorders of neurological development. The size of each solid circle represents the sample size of each study. The regression SROC curve indicates the overall diagnostic.

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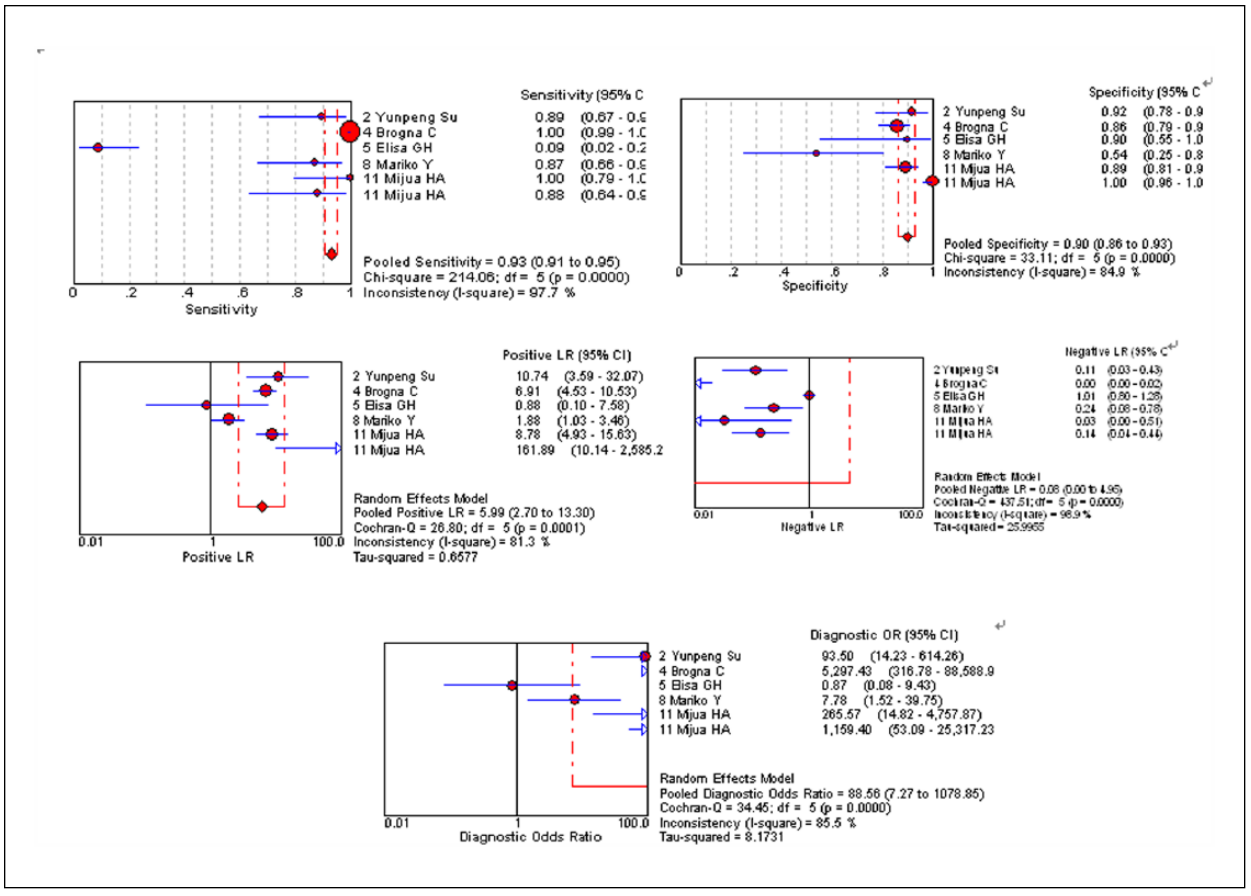

Figure 6. Forest plots of sensitivity and specificity for general movements (GMs) in the diagnosis of fidgety disorders of neurological development. The point estimates of sensitivity and specificity from each study are shown as solid circles. Error bars indicate 95% confidence intervals (CIs).

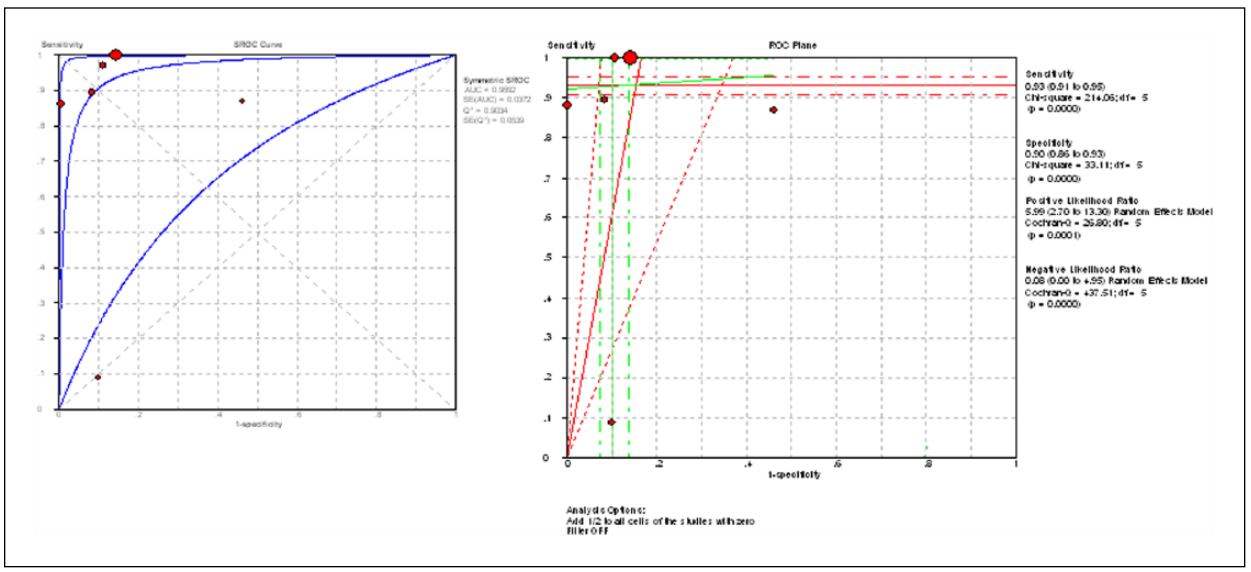

Figure 7. Summary receiver operating characteristic (SROC) curve of general movements (GMs) in the diagnosis of fidgety disorders of neurological development. The size of each solid circle represents the sample size of each study. The regression SROC curve indicates the overall diagnostic.

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Discussion

The assessment of GMs during the first 20 weeks is a new method for early detection of neurodevelopment disorders and brain dysfunction. Usually, GMs occur just after birth to 18 to 20 weeks postterm. These complex movements of the head, trunk, and limbs are characterized by variability in speed, amplitude, force, and intensity.[10,15,16] Usually, very few children developing attention problems showed abnormal movements at neurological examination during infancy. The quality of the GMs contributed more to prediction than the ultrasound findings.[8,17]

The present meta-analysis investigated the overall diagnostic value of GMs in the diagnosis of neurological development. The finding supports the notion that the quality of GMs may provide useful information in detecting abnormal neurodevelopment, especially for fidgety period and for CP outcome. The analysis toward GMs in the writhing period showed that the sensitivity of GMs assessment was 0.91, indicating a potential role for GMs assessment in the confirmation of abnormal neurological development. In contrast to the high sensitivity, the specificity was only 0.74, which is insufficient to excluding the patients without disorders. Thus, positive tests do clearly indicate the existence of disorders of neurological development, and patients with positive results have a fairly low chance of not having disorders. The PLR and NLR were also determined as measures of diagnostic accuracy in the present study, as likelihood ratios are considered to be more clinically meaningful than the diagnostic odds ratio (DOR).[18-20] A PLR value of 2.87 in the present study suggested that patients with neurological development disorders have ~3-fold higher chance of testing positive in the GMs assessment than patients without the disorders, which should be helpful in clinical practice. However, the NLR value of 0.19 determined in the present study meant that if the GMs assessment result was negative, the probability that a patient was affected by neurological development disorders was ~20%. The DOR, which is the ratio of the odds of a positive test result in the diseased relative to that in the nondiseased state, is an alternative indicator of test accuracy. The higher the DOR value, the more discriminatory the test. In the present meta-analysis toward GMs assessment in predicting disorders of neurological development, the mean DOR was found to be 16.36, suggesting that GMs assessment is a useful tool for aiding the diagnosis. The Q-value is a global measure of test efficacy. It is the point of intersection of the SROC curve with a diagonal line from the left upper corner to the right lower corner of the ROC space, and corresponds to the highest common value of sensitivity and specificity for the test. This point not only indicates the best combination of sensitivity and specificity for a particular clinical setting but also represents an overall measure of the discriminatory power of a test. To summarize the test performance, an SROC curve was generated, which indicates the balance between sensitivity and specificity. The SROC curve for the present meta-analysis revealed that the maximum joint sensitivity and specificity (Q-value) was 0.80 and the AUC was 0.87, indicating that the overall accuracy was not very high.

The analysis toward GMs in the fidgety period showed that the sensitivity of GMs assessment was lower than in writhing period, indicating a potential role for GMs assessment in the confirmation of abnormal neurological development was not so good. The specificity was only 0.09, which is insufficient to exclude the cases without disorders. Thus, positive tests do not clearly indicate the existence of disorders of neurological development, and patients with positive results have a fairly high chance of not having the disorders. The PLR and NLR in the present study were 6.97 and 0.07, respectively, which suggested that patients with neurological development disorders have almost a 7-fold higher chance of testing positive in the GMs assessment than patients without the disorders, which should be helpful in clinical practice. The NLR value of 0.07 in the present study meant that if the GMs assessment result was negative, the probability that a patient was affected by neurological development disorders was only ~7%. However, the DOR was found to be 122.79, suggesting that GMs assessment is helpful in the diagnosis. The SROC curve for the present meta-analysis revealed that the maximum joint sensitivity and specificity (Q value) was 0.914 and the AUC was 0.9664, indicating that the overall accuracy was rather good.

Apart from the abnormal outcome of neurological development for writhing and fidgety periods, CP was also another important factor in judging the disorders of neurological development. The present study also analyzed the diagnostic value of GMs assessment in diagnosing CP. The results were similar as the value of GMs in diagnosing writhing period neurological development disorders. The sensitivity of GMs assessment was 0.93, which was good for confirmation of the abnormal neurological development. The specificity was 0.54, which is insufficient to exclude the disorders. The PLR and NLR in the present study were 5.99 and 0.08, respectively, suggesting that patients with neurological development disorders have about 6-fold higher chance of testing positive in the GMs assessment than patients without the disorders, and the probability that a patient was affected by neurological development disorders was only ~8%. The DOR was found to be 88.56, suggesting that GMs assessment is helpful in the diagnosis. The SROC curve for the present meta-analysis showed that the maximum joint sensitivity and specificity (Q value) was 0.9034 and the AUC was 0.9592, indicating that the overall accuracy was good.

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In summary, GMs assessment resulted in few false positives in the diagnostic test for writhing neurological outcome and CP. The predictive power of the abnormal infant fidgety neurological examination outcomes and CP results were rather high. Thus, with significantly good sensitivity in the detection of neurological development, GMs evaluation is likely to be an effective method to ascertain the potential existence of disorders. However, ruling out neurological development by evaluation of GMs alone is not recommended because of its limited specificity, and the results should be interpreted in parallel with conventional test results and other clinical findings. However, the present study had certain limitations. First, studies published in languages other than English and Chinese, unpublished studies, and abstracts from conference proceedings were not included. Second, issues such as the exact condition of the patients and laboratory infrastructure were not analyzed because of limited data.

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Author Contributions

BM contributed to the conception and design and gave final approval of the manuscript to be published. KX carried out the conception and design of the study, as well as analysis of the data and drafting and revising the manuscript. HZ, HuL,CZ, HL and HJ participated in the manuscript conception and selection of the included studies.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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