Author's response to reviews

Title: Predicting neurodevelopmental outcomes for at-risk infants: reliability and predictive validity using a Chinese version of the INFANIB at 3, 7 and 10 months

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Author's response to reviews: see over
Dear Dr. Crow:

Thank you for reviewing our report titled “Predicting neurodevelopmental outcomes for at-risk infants: reliability and predictive validity using a Chinese version of the INFANIB at 3, 7 and 10 months.” The editor’s and reviewers’ comments helped us to make appropriate revisions to our manuscript. We appreciate the opportunity to make these revisions and to resubmit our manuscript for your further consideration. Below is our point-by-point response to the editorial and reviewers’ comments.

Response to Editorial comments:

Editor’s comment:
Ethics - Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/e/policy/b3.htm), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

Response: We have added the appropriate statement that this project has been approved by Institutional Reviewer Board of 2nd affiliated hospital of the Third Military Medical University, China in December 6, 2007 (Approval No. 2007082).

Editor’s comment:
Consent - Informed consent must also be documented. Manuscripts may be rejected if the editorial office considers that the research has not been carried out within an ethical framework, e.g. if the severity of the experimental procedure is not justified by the value of the knowledge gained.

Response: We have added the appropriate statement to the Methods section under Subjects. Signed informed consents were obtained from the parents of minor subjects who participated in this project.
Editor’s comment:
Abstract - Please could you structure your abstract according to the guidelines provided at this page: http://www.biomedcentral.com/info/ifora/abstracts. Specifically, we request that you add Background information to the abstract. Please also ensure that your revised manuscript conforms to the journal style(http://www.biomedcentral.com/info/ifora/medicine_journals ). It is important that your files are correctly formatted.

Response: We have added the Background statement to the Abstract according to the guidelines and have rechecked all other formatting as requested.

Response to reviewers’ comments:

Reviewer’s comment:
These are my comments to the “Predicting neurodevelopmental outcomes for at-risk infants: reliability and predictive validity using a Chinese version of the INFANIB at 3, 7 and 10 months” Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore). Please attach your Chinas version and the administrartion guidline.

Response: We have attached the Chinese version of the INFANIB as requested.

Reviewer comment:
The results of US Scans must be come to result section ( not in the method).

Response: We have made sure that the ultrasound scan information is included only in the Results section as advised.

Reviewer’a comment:
In discussion section one of the reasons of low validity for 3 months infants is that the INFANIB is the neurodevelopmental scale of 4-18 months old and the validity of test increase with age.

Response: We have modified this statement in the Discussion section, second paragraph, and added an appropriate citation to help explain the low validity for 3-month-old infants. In fact, the children participating in the study during development of the INFANIB in 1985 were aged from 3 months to 22 months (14). This might be one of the reasons that low validity for 3 months infants was observed in this study. This has been noted in our report accordingly.

Reviewer’s comment:
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Reviewer’s comment:
The first paragraph in reliability section is better transfer to statistical analysis. An ICC>0.90 shows high reliability, 0.75-0.90 reveals good reliability, 0.50-0.75 displays intermediate reliability and <0.05 suggests poor reliability.

Response: The information was moved to the Statistical Analysis paragraph as suggested.

Reviewer’s comment:
Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Revision of the result section of the abstract

Response: The Results section of the Abstract summarizes results of the study. P values and other data were included where applicable to support summary statements. We have checked all results against the Tables and revised as needed for consistency.

Reviewer comment:
Determine that these psychometric properties accurate only in high risk infants in your discussion and abstract.

Response: We have made sure that validity and reliability are reported only for the INFANIB as it applies to high-risk infants as reported in the Discussion and Abstract.

Reviewer comment:
Describe all your terminology in the method such as HIE, asphyxia, brain damage, intracranial hemorrhage, maternal hypertension and so on.

Response: We have defined the following terms in the Methods section under Definitions:
Hypoxic ischemic encephalopathy (HIE)
Asphyxia
Intracranial hemorrhage
Brain damage
Maternal hypertension during pregnancy (pregnancy induced hypertension)
Periventricular leukomalacia (PVL)

Reviewer’s comment:
Describe on PDMS and the evaluated items with it.
Response:
To date, PDMS has been a widely applied scale for comprehensive evaluation of motor function in the field of rehabilitation and early intervention in children. PDMS is suitable for the evaluation of motor development (including motor development disorder of any cause) in children aged 6~72 months. We have cited the studies for the PDMS pilot version, the PDMS 2nd edition (PDMS-2) and the reliability and validity of PDMS-2 Chinese version, which was reported by Yang et al. in 2010 (in Chinese). The Methods section already describes the PDMS and how it was applied in this study. However, we have added a more comprehensive explanation of the PDMS in the Methods section describing its construction. Please see the revised Methods section.

Reviewer comment:
Does PDMS diagnose CP? As you say in the table 3 and 4. Abnormal in PDMS includes cerebral palsy or movement retardation (GMQ .79).

Response:
The PDMS cannot be used to diagnose cerebral palsy. As shown in Table 3 and 4, the children with abnormal scores in PDMS evaluation included the children with movement retardation and those with cerebral palsy, who definitely have poor scores. The important point is that not all children with movement retardation have cerebral palsy. Some children with movement retardation do not meet the criteria for cerebral palsy. We have revised the explanation in both the Results section and the Discussion section to clarify the issue. Please see the revised sections.

Reviewer comment:
What is the unclear diagnosis with INFANIB? As you have normal, transient and abnormal groups by this scale.
“The presence of CP or GMQ .79 on the PDMS-2 was considered as a motor development disorder. Abnormal and transient” on INFANIB assessment was defined as positive for neuromotor developmental disorders and “normal” on INFANIB assessment was defined as negative for neuromotor developmental disorders. When the results were unclear, infants were followed up and rehabilitation was recommended without help from professionals; those infants were also defined as negative for neuromotor developmental disorders. The sensitivity, specificity, PPV and NPV were calculated accordingly. “

Response: There is no motor development delay that INFANIB is unable to assess. The sentence in the Methods section that says: “When the results were unclear” was revised to say: “When the results were transient.” We were referring to transient results. Please see the revised Methods.

Reviewer comment:
If you have rehabilitation by family in 12-24 months, how you had diagnosis for CP by <79 PDMS Score.
**Response:** This seems to be asking how CP can be diagnosed with a PDMS score of <79 during the 12-24-month rehabilitation at home. Again, The PDMS cannot be used to diagnose cerebral palsy solely. Generally, at least 1 year after the birth (about 12~24 months; corrected age for premature infants), pediatricians can evaluate the motor outcome based on the PDMS-2. At the same time, the developmental pediatricians diagnose CP based on severe abnormal motor development. If the diagnosis of CP is not definite, follow up will be needed. The motor outcome will be determined during the follow-up performing repeated PDMS-2 evaluations and applying the maximal score. A PDMS-2 score of <79 was also used as an indicator of abnormal outcome of neurological development. Once the score in PDMS-2 evaluation was normal and neurological examination also excluded abnormalities, the neurological development was then defined as normal. We have added further explanation to the Methods section under Subjects and under the PDMS section “Determination of gross motor development outcomes by PDMS.”

Reviewer comment:

The result section must be revised, because the data on tables have repeated in results.

**Response:** We have modified the Results section and removed data repeated from the Tables as requested. Please see the revised Results section.

Reviewer comment:

Whats your mean of Apgar score of 0-3 mean as asphyxia and 4-7 as severe asphyxia? “scores (0-3 within 1 minute of birth is defined as asphyxia, 4-7 is severe asphyxia)”

**Response:** We have revised the statement accordingly to: Asphyxia is considered in infants with a 5-min Apgar score of 0–3. In the Discussion section, we have revised text and added a citation to help support the identification of asphyxia using Apgar scores.

Reviewer comment:

Minor Essential Revisions In this revised version, the authors were able to respond satisfactorily to some of the queries, criticisms and suggestions of the referee. The overall quality of the paper has been improved with few points to clarify:

Reviewer comment:

Introduction: Line 8-9 "when brain plasticity is the most potent.." use the sentence "due to brain plasticity"

**Response:** We have revised that sentence accordingly.

Reviewer comment:

Methods: subjects, line 5: the description of US findings should be added in results only.

**Response:** We have made sure that the ultrasound imaging results are only described in the
Results section.

Reviewer comment:

page 6 line 1: delete "using auxology"; line 2: remove the sentence "Premature infants comprise a.... and behavioral disorders [17]." and add in the introduction.

Response: We have revised that sentence as advised. The statement about “premature infants comprise...” has been moved to the Background section (Introduction) as requested.

Reviewer comment:

Results
page 9, last sentence: delete "according to the INFANIB scores"

Response: We have deleted the phrase accordingly.

Reviewer comment:

Reference of PDMS evaluation.

Response: As described above, we have added a more comprehensive explanation of the PDMS-2 to the Methods section under Subjects and under the PDMS section “Determination of gross motor development outcomes by PDMS.” We have referenced the text with Folio et al., 2000; Palisano et al., 1995; and Yang et all 2010, who validated the Chinese version of the scale. Please see these revised sections.

Reviewer comment:

Discussion
page 12-13: the criteria to define Asphyxia shuold be added in methods only.

Response: Asphyxia has been defined in the Method section as “Infants with a 5-min Apgar score of 0-3.” Please see the revised Methods section under Definitions.

This concludes our response to the reviewers’ comments. Thank you for this opportunity to resubmit our study for reconsideration of publication in BMC Pediatrics.

Sincerely,

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