Clinical application of Chinese Nanjing persistent vegetative state scale

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Abstract

Background: It is a challenge to characterize the consciousness level of patients with severe disturbance of consciousness and predict their prognosis effectively for Chinese doctors. We aimed to investigate the psychometric property and the diagnostic practicality of severe disturbance of consciousness by Chinese Nanjing persistent vegetative state scale (CNPVSS) which was first set up in 1996 and modified in 2001 and 2011.

Methods: The concurrent validity, inter-rater consistency and diagnostic accuracy of CNPVSS and Chinese version of coma recovery scale-revised (CRS-R) were investigated by assessment of 380 patients with severe disorders of consciousness.

Results: Total scores of the CNPVSS were correlated significantly with that of the CRS-R, indicating acceptable concurrent validity. Sub-scale analysis showed moderate to high inter-rater reliability and test-retest reliability. CNPVSS was superior to CRS-R on the diagnosis sensitivity. The CNPVSS was able to distinguish 65 patients in emergence from minimal consciousness state who were misclassified as in minimal consciousness state (MCS) by the CRS-R, and it could also distinguish two patients in MCS who were misclassified as in vegetative state by the CRS-R.

Conclusion: The CNPVSS is an appropriate measurement and is sensitive to distinguish the MCS patients from the VS patients.

Keywords: Chinese Nanjing persistent vegetative state scale; Coma recovery scale-revised; Emergence from minimal consciousness state; Minimal consciousness state; Severe disorders of consciousness; Unresponsive wakefulness syndrome; Vegetative state

Introduction

In recent years, with the development of intensive care and the increase of traumatic cerebral injury patients, the number of patients with severe disturbance of consciousness is growing.[1] It is still a main problem to characterize patients’ consciousness level and predict their prognosis effectively.[2,3] In vegetative state (VS), there could be possible wakefulness recovery but with no evidence of perception conscious behaviors.[4] In 2002, some specialists used the term “minimal consciousness state (MCS)” to describe a remarkable sign of a little better consciousness state than unconsciousness state.[5] MCS is characterized by clearly discernible behavioral signs of conscious awareness. For example, visual pursuit, movement to simple command, and yes-no communication by gesture. These behavior changes are too subtle for inspectors to estimate the consciousness state of patients with objective methods, but only by repeated behavior detection and meticulous observation.[6] Therefore, it is important to distinguish patients with subtle signs of conscious behavior from those without any sign of consciousness timely and accurately.

It has been shown that conventional scales had a high misdiagnosis rate of 37% to 43%.[7] The misdiagnosis affected patients’ management and the decision whether to give up therapy. So we need a more sensitive measurement scale. Coma recovery scale-revised (CRS-R) is a common accepted diagnosis instrument improved by the Aspen

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working group to evaluate the consciousness state of patients with disorders of consciousness (DOC). On the basis of case analysis, we initially described the Chinese version of CRS-R in 2013, which had been internationally recognized. And in China, a group of top doctors of Neurology, Neurosurgery, Emergency Medicine and hyperbaric oxygen Medicine set up the Chinese Nanjing persistent vegetative state scale (CNPVSS) in 1996, which was used to evaluate the consciousness state of patients with DOC. The CNPVSS was modified in 2001 and 2011, respectively, based on clinical feedback. This study aimed to explore the internal consistency, concurrent validity, and diagnostic accuracy between CNPVSS and CRS-R.

**Methods**

**Ethical approval**

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee of the institute. Written informed consent was obtained from the participants’ legal guardians before enrollment.

**Assessment scales**

The Chinese version of CRS-R consists of 25 hierarchically arranged items that comprise six sub-scales addressing arousal, auditory, visual, motor, oromotor/verbal, and communication function. Total scores: 0 to 23.

CNPVSS was finalized in Nanjing with the help of the Cerebral Resuscitation Professional Board in 2011. It also consists of 25 hierarchically arranged items that comprise five sub-scales addressing limb movement, eyes, audition, feeding and emotion items. Total scores: 0 to 20.

**Participants**

The prospective study included 380 DOC patients from May 2015 to February 2016, 238 males (63%) and 142 females (37%), aged between 33 and 64 years. The time of consciousness disturbance existed more than 30 days. All the patients were diagnosed with the CRS-R criteria. The etiology of DOC: traumatic 161 (42%), non-traumatic 219 (58%) cases, the periods of post-injury were between 1.31 and 17.37 months. Patients and non-traumatic 219 (58%) cases, the periods of post-injury were between 1.31 and 17.37 months. Patients were recruited from six hospitals, including Nanjing Zijin Hospital, the Third People’s Hospital of Chengdu, Research Institute on Consciousness Disturbance of Hangzhou Normal University, Armed Police Hospital of Hangzhou, Guangdong 999 Brain Hospital and Heilongjiang Convalescent Hospital, according to the following inclusion criteria: ≥18 years, classified in VS/unresponsive wakefulness syndrome (UWS) (VS was also called UWS) or MCS by CRS-R, recorded acquired brain injury, and no following drugs administered within 48 h before the assessment; central stimulant, neuromuscular blocking agent, and sedative. Exclusion criteria: (1) patients’ vital signs were unstable and not suitable for assessment, documented history of brain injury before the one causing DOC, (2) there was a history of mental retardation, refractory epilepsy, and severe mental disorders leading to DOC.

**Procedures**

There were 12 evaluators, two for each hospital who should evaluate the patients respectively to minimize bias. Before the study, we conducted a 3-month unified training for all the evaluators participating in the experiment from the six hospitals to minimize the differences between individuals. During the examination, we should ensure sufficient arousal level of the patients. Both CRS-R and CNPVSS scales were applied in a single session. With convenience sampling method, examiners performed the bedside testing. Before the formal assessment, each session started with a 3-min baseline observation, recorded the patient’s basic condition and scoring of the spontaneous behaviors at rest according to the CRS-R and CNPVSS guidelines. On day 1, rater A examined the patient in the morning, and rater B examined the patient in the afternoon. On the second day, the previous day’s work was repeated.

In Chinese version of CRS-R and CNPVSS, the lowest item on each sub-scale only represented reflexive activity, while the highest item represented cognitive and consciousness-mediated activities. The evaluation process included baseline observation, innocent stimulation, and noxious stimulation. Because auditory, visual, and limb movement were available on both scales, these sub-scales were evaluated first. We used sound stimulation, visual stimulation, and pain stimulation to evaluate patient reaction. Then we evaluated verbal, communication, arousal level, feeding, and emotion, respectively. Table 1 was a comparative description of both scales.

**Statistical analysis**

**Internal analysis of CNPVSS**

Cronbach α coefficient was used to measure the internal consistency of CNPVSS, and internal consistency among its sub-scales was further explored through either Pearson or Spearman correlation coefficients.

**Inter-rater reliability**

The intra-class correlation coefficient (ICC) was used to assess the inter-rater agreement of the CNPVSS. Fifty patients were enrolled in the inter-rater agreement study. Rater A’s scores in the morning were compared with rater B’s scores in the afternoon on the same day (time interval <12 h). Then we could get an ICC and determine the inter-rater agreement.

**Test-retest reliability**

The test-retest reliability was explored by consistency analysis of the scores obtained from different days. 380 patients were enrolled. We got the ICC from the two total scores provided at two different times by a single rater (the interval time was one day, without central stimulant,
neuromuscular blocking agent, and sedative), with which the test-retest reliability of CNPVSS was estimated.

**Concurrent validity**

The CRS-R or the CNPVSS was administered to all 380 patients by skilled rater A in a random order to investigate validity, total CRS-R scores were compared with total CNPVSS scores. According to the distribution of the data, Kendall-tau correlation coefficient statistic was used to explore the concurrent validity of the CNPVSS.

**Table 1: Description of items included in the CRS-R and CNPVSS.**

| Sub-scale               | CRS-R                                                                 | CNPVSS                                                                 |
|------------------------|----------------------------------------------------------------------|------------------------------------------------------------------------|
| Auditory               | ★4-Consistent movement to command                                   | ★4-Movement to complicated command                                      |
|                        | ★3-Reproduction movement to command                                 | ★- Reproduction movement to simple command                               |
|                        | 2-Sound localization                                                 | ★2-Localization to sound; occasionally movement to simple command      |
|                        | 1-1-Auditory startling                                              | 1-Eye opening with sound stimulation                                   |
|                        | 0-None                                                               | 0-None                                                                 |
| Visual/eye movement    | ★5-Object recognition                                               | ★4-Identifying objects                                                  |
|                        | ★4-Object localization (reaching)                                   | ★-Object localization (reaching)                                       |
|                        | ★3-Visual pursuit                                                   | ★2-Visual pursuit                                                      |
|                        | ★2-Fixation (>2 seconds)                                            | 1-Object arouse, vigilance                                              |
|                        | 1-Visual startle (startle reaction)                                 | 0-None                                                                 |
|                        | 0-None                                                               |                                                                        |
| Motor/limb movement    | ★6-Functional object use                                            | ★4-Voluntary movement, can complete more complex random behaviors     |
|                        | ★5-Automatic motor response                                         | ★- Object manipulation                                                 |
|                        | ★4-Object manipulation                                              | ★2-Location and dodge to stimulation                                    |
|                        | ★3-Flexion to noxious stimulation                                   | 1-Flexion and extension reaction with stimulation                      |
|                        | 2-Flexion withdraw                                                  | 0-None                                                                 |
|                        | 1-Abnormal posturing                                                |                                                                        |
|                        | 0- None/flaccid                                                     |                                                                        |
| Oromotor/verbal        | ★3-Intelligible verbalization                                       | NA                                                                     |
|                        | 2-Vocalization/oral movement                                        |                                                                        |
|                        | 1-Oral reflexive movement                                           |                                                                        |
|                        | 0-None                                                               |                                                                        |
| Communication          | ★2-Functional (accurate)                                            | NA                                                                     |
|                        | 1-Non-functional (intentional)                                      |                                                                        |
|                        | 0- None                                                             |                                                                        |
| Arousal level          | ★3-Attention                                                        | NA                                                                     |
|                        | 2-Eye opening                                                       |                                                                        |
|                        | 1-Eye opening with stimulation                                      |                                                                        |
|                        | 0-None                                                               |                                                                        |
| Feeding                | NA                                                                  | ★4-Automatic taking food                                               |
|                        |                                                                     | ★- Full diet                                                           |
|                        |                                                                     | ★2-Swallowing, movement to simple command                              |
|                        |                                                                     | 1-Swallowing                                                           |
|                        |                                                                     | 0-None                                                                 |
| Emotion                | NA                                                                  | ★4-Normal emotional reaction                                           |
|                        |                                                                     | ★- Have complicated reaction                                          |
|                        |                                                                     | ★2-Weeping excitement, suffering can be found                          |
|                        |                                                                     | 1-Sometimes performs of excitement (BP; R; HR increasing)              |
|                        |                                                                     | 0-None                                                                 |

CRS-R: Coma recovery scale-revised; CNPVSS: Chinese Nanjing persistent vegetative state scale; NA: Not applicable; BP: Blood pressure; R: Respiration; HR: Heart rate. ★ represents minimal consciousness state, MCS. ★ represents emergence from minimal consciousness state, EMCS.

**Diagnostic accuracy**

Aspen criteria of the VS and MCS are composed of behavioral items of the CRS-R. The purpose of using CRS-R is to identify patients with subtle signs of consciousness. The diagnostic criteria of two scales are shown in Table 2 and Table 3.

These criteria were taken as diagnostic criteria for the 380 patients. We used the Chi-squared test as well as Kendall tau-b coefficient to determine the consistency between Chinese CRS-R and CNPVSS.
The prospective study included 380 DOC patients, diagnosed with the CRS-R criteria: 238 males (63%), 142 females (37%), aged between 33 and 64 years (mean age: 48.65 ± 14.90). The etiology of DOC was traumatic in 161 (42%) and non-traumatic 219 (58%). Time after injury was between 1.31 and 17.37 (mean age: 9.34 ± 8.03) months.

Internal consistency of CNPVSS

The standardized Cronbach α coefficient of CNPVSS is 0.895. The results of sub-scale on internal consistency are shown in Table 2.

| Items         | Limb movement | Eye movement | Auditory | Feeding | Emotion |
|---------------|---------------|--------------|----------|---------|---------|
| Limb movement | 1.000         | –            | –        | –       | –       |
| Eye movement  | 0.769         | 1.000        | –        | –       | –       |
| Auditory      | 0.821         | 0.788        | 1.000    | –       | –       |
| Feeding       | 0.536         | 0.460        | 0.594    | 1.000   | –       |
| Emotion       | 0.574         | 0.602        | 0.630    | 0.605   | 1.000   |

* P < 0.05.

Table 3: The inter-rater agreement and test-retest reliability of sub-scales with Chinese Nanjing persistent vegetative state scale (N = 380).

| Item         | CNPVSS limb | CNPVSS eye | CNPVSS auditory | CNPVSS feeding | CNPVSS emotion | CNPVSS diagnosis |
|--------------|-------------|------------|-----------------|----------------|----------------|------------------|
| Inter-rater ICC | 1.000*      | 1.000*     | 0.991*          | 1.000*         | 0.984*         | 1.000*           |
| Test-retest ICC | 0.993†      | 1.000†     | 0.981†          | 0.983†         | 0.999†         | 1.000†           |

* P < 0.05; † P < 0.01. ICC: Intra-class correlation coefficient.

Table 4: Diagnostic results by using the CNPVSS and CRS-R.

| CRS-R | VS     | MCS    | EMCS   | Total |
|-------|--------|--------|--------|-------|
| VS    | 215    | 6      | 0      | 221   |
| MCS   | 4      | 90     | 65     | 159   |
| EMCS  | 0      | 0      | 0      | 0     |
| Total | 219    | 96     | 65     | 380   |

Chi-square = 340.75, P < 0.001, Kendall tau-b coefficient is 0.882 (P < 0.001) and it indicates sound consistency among diagnostic results by using the CNPVSS and CRS-R. CNPVSS, Chinese Nanjing persistent vegetative state scale; CRS-R, Coma recovery scale-revised; VS, vegetative state; MCS, minimal consciousness state; EMCS, emergence from minimal consciousness state.

Results

The prospective study included 380 DOC patients, diagnosed with the CRS-R criteria: 238 males (63%), 142 females (37%), aged between 33 and 64 years (mean age: 48.65 ± 14.90). The etiology of DOC was traumatic in 161 (42%) and non-traumatic 219 (58%). Time after injury was between 1.31 and 17.37 (mean age: 9.34 ± 8.03) months.

Internal consistency of CNPVSS

The standardized Cronbach α coefficient of CNPVSS is 0.895. The results of sub-scale on internal consistency are shown in Table 2.

A moderate to high internal consistencies were identified among sub-scales of CNPVSS, correlation coefficients range from 0.46 to 1.

Inter-rater consistency

High inter-rater agreement was observed among all sub-scales within CNPVSS, with ICC ranges from 0.984 to 1 [Table 3].

Test-retest reliability

High test-retest reliability was found among all sub-scales within CNPVSS, with ICC ranges from 0.981 to 1 [Table 3].

Concurrent validity

Total scores of the CRS-R correlated with total score of the CNPVSS were used to establish concurrent validity. The Kendall-tau correlation coefficient is 0.879 (P < 0.001).

Diagnostic accuracy

Each patient was diagnosed as VS/UWS, MCS, or emergence from minimal consciousness state (EMCS) after completion of the CNPVSS and Chinese CRS-R. The diagnostic results by using the CNPVSS and CRS-R are shown in Table 4.

Discussion

Accurate diagnosis of patients with severe DOC is crucial for prognostic validity and medical management but remains challenging. DOC that can be presented by patients with severe brain injury include a wide range of consciousness states.[10,11] Since the definition in 2002,[4] MCS has been studied to be distinguished from VS.[12] Diagnostic inaccuracies and misdiagnosis remain common, and high misdiagnosis rate of conventional scales made it urgent to find a more sensitive measurement scale. CRS-R is an validated diagnosis instrument to distinguish MCS from VS.[8] We first described the internationally recognized Chinese version of CRS-R in 2013.[9] CNPVSS was set up in 1996 and modified in 2001 and 2011 to evaluate the consciousness state of severely brain injured patients. In this study, we explored the concurrent validity, internal consistency, and diagnostic accuracy of the CNPVSS.

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In CNPVSS, we added emotional experience and feeding sub-scales, removed the three parts of verbal expression, communication and arousal in CRS-R, and evaluated the levels of consciousness from the physiological function to the advanced cognitive processes. Through the assessment of emotions, we were able to understand the internal perception of the patient, rather than limiting ourselves to the external perception of the patient’s perception of the outside world. Removing verbal expression and communication could avoid the distortion of the scores due to tracheotomy, aphasia, and so on.

The Cronbach α coefficient was 0.895, indicating a good internal consistency and psychometric property of CNPVSS. High ICCs of the limb, eye, auditory, and emotion sub-scales showed high inter-rater reliability of the CNPVSS sub-scales. High ICCs of the limb, eye, auditory, feeding, and emotion sub-scales demonstrated adequate test-retest reliability of the five sub-scales.

Total scores of the CRS-R were closely related to total scores of the CNPVSS with Spearman coefficient \( r = 0.879 \), indicating a strong association between the CNPVSS and the CRS-R. The CNPVSS distinguished 65 patients in EMCS who were misclassified as in MCS by CRS-R and two patients in MCS who were misclassified as in VS by the CRS-R, indicating higher diagnosis accuracy of CNPVSS than CRS-R.

In summary, both the CNPVSS and the CRS-R are appropriate measurement for characterizing consciousness level. When compared with CRS-R, the CNPVSS is more sensitive to distinguish the MCS patients from the VS patients. The CNPVSS demonstrated good inter-rater reliability, psychometric property, and adequate inter-rater, test-retest reliabilities of the sub-scales.

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**Conflicts of interest**

None.

**References**

1. Laureys S, Boly M. The changing spectrum of coma. Nat Clin Pract Neurol 2008;4:544–546. doi: 10.1038/ncpneuro0887.
2. Wang ZM. Psychological Research Methods. 2nd ed. Beijing: People’s Education Press; 2001. 134–146.
3. Fei LP. Evaluation and Revision of the Western Scale. The Mental Health Scale Handbook (Revised Edition). Beijing: China Mental Health Journal; 1999. 427–436.
4. Ashwal S, Cranford R. Medical aspects of the persistent vegetative state—a correction. The multi-society task force on PVS, N Engl J Med 1995;333:130. doi: 10.1056/NEJM199507133330217.
5. Giacino JT, Ashwal S, Childs N, Cranford R, Jennett B, Katz DL, et al. The minimally conscious state: definition and diagnostic criteria. Neurology 1993;43:1465–1467.
6. Andrews K, Murphy L, Munday R, Littlewood C. Misdiagnosis of the vegetative state: retrospective study in a rehabilitation unit. BMJ 1996;313:13–16. doi: 10.1136/bmj.313.7048.13.
7. Giacino JT, Kalmar K, Whyte J. The JFK coma recovery scale-revised: measurement characteristics and diagnostic utility. Arch Phys Med Rehabil 2004;85:2020–2029. doi: 10.1212/WNL.58.3.349.
8. Zhang Y, He HM, Zhao FL, Feng GH, Wang WM, Qui WS, et al. Reliability and validity of Chinese version of CRS-R scale. Nurs Rehabil 2013;12:715–717. doi: 10.3969/j.issn.1671-9875.2013.08.001.
9. Schnakers C. Clinical assessment of patients with disorders of consciousness. Arch Ital Biol 2012;150:36–43. doi: 10.4449/aiib.v150i1.1371.
10. Piguet JM, Mauron E, Jöhr J, Gilart de Keranflec’h G, Van De Ville D, Preti MG, et al. Outcome prediction of consciousness disorders in the acute stage based on a complementary motor behavioural tool. PLoS One 2016;11:e0156882. doi: 10.1371/journal.pone.0156882.
11. Laureys S, Celesia GG, Cohadon F, Lavriven J, León-Carrion J, Sannita WG, et al. Unresponsive wakefulness syndrome: a new name for the vegetative state or apalic syndrome. BMC Med 2010;8:68. doi: 10.1186/1741-7015-8-68.