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Mandarin Validation of the Simplified Evaluation of CONsciousness Disorders (SECONDS)

--Manuscript Draft--

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Abstract:	Background. The Simplified Evaluation of CONsciousness Disorders (SECONDS) was recently proposed as a new fast scale to accurately diagnose patients suffering from disorders of consciousness (DoC). The aim of this study was to translate the SECONDS into Mandarin and validate it in a sample of Mandarin-speaking patients with DoC. Methods. Each patient was assessed by three distinct assessors. All assessments were completed within two weeks (7 SECONDS and 5 CRS-R). Until the end of the protocol, all three assessors were blinded to the scores acquired by the other assessors. Results. In the 47 included participants, the concurrent validity between diagnoses made with the CRS-R and the SECONDS on the same day or the best diagnoses between CRS-R and SECONDS led to "substantial" agreement (kappa from 0.61 to 0.72). Intra-/inter-rater reliability also showed almost perfect/substantial agreement (kappa from 0.90 to 0.91 and 0.75 to 0.76, respectively). Conclusions. The Mandarin version of the SECONDS has almost perfect reliability and substantial validity.



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Annals of Physical and Rehabilitation Medicine

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Dear Professor Dominic Pérennou:

On behalf of all authors, I would like to ask you to consider our manuscript entitled “Mandarin Validation of the Simplified Evaluation of CONsciousness Disorders (SECONDS) ” for publication in Annals of Physical and Rehabilitation Medicine as an original research article.

The work described has not been submitted elsewhere for publication, in whole or in part, and all the authors listed have approved the manuscript that is enclosed.

This work aims to provide a reliable scale (Simplified Evaluation of CONsciousness Disorders in Mandarin Chinese language) to assess patients with disorders of consciousness. Repeated Coma Recovery Scale-Revised (CRS-R) evaluation is recommended for patients with disorders of consciousness, but its time-consuming administration is a challenge given the workload of medical staff. A fast and convenient scale is urgently needed to decrease the assessment duration and lower misdiagnosis rates. In this setting, the Simplified Evaluation of CONsciousness Disorders (SECONDS) exactly meet these needs.

We have no conflicts of interest to disclose.

word count for main text : 1800, number of tables : 1, number of figures : 2

We deeply appreciate your consideration of our manuscript, and we look forward to receiving comments from the reviewers. If you have any queries, please don't hesitate to contact me at the address below. Correspondence should be directed to Haibo Di at the following address:

Sincerely yours



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We would like to thank you for your careful reading, helpful comments, and constructive suggestions, which have significantly improved our manuscript.

We have carefully considered all comments from the reviewers and revised our manuscript accordingly. The manuscript has also been double-checked for English language, and the errors we found have been corrected. In the following section, we summarize our responses to each comment from the reviewers. We believe that our responses have well addressed all concerns from the reviewers. We hope our revised manuscript can be accepted for publication.

Reviewer #1: '

This letter has 2 aims:

- Translate de French version of the SECONDS
- Assess the concurrent validity compared to the gold standard CRS-R, test intra- and inter-rater reliability of the Chinese version of the SECONDS

The methodology seems relevant for both aims and the results provide further convincing evidence that the SECONDS (in its Chinese version) is a valid and reliable scale, faster than the CRS-R (actual gold standard), to discriminate unresponsive wakefulness syndrome (UWS) versus minimally conscious state (MCS).

Comment: My main concern for a publication in the Annals of Physical and Rehabilitation Medicine is the sufficient novelty given that concurrent validity and intra- and inter-reliability of the SECONDS (French version) have already been published (Aubinet et al., APRM 2021).

➤ **Reply:**

Behavioral research often lacks high-quality translations with standardized translation processes, and we humbly hope a journal like APRM would encourage the publication of robust and qualitative research that spreads the linguistic scope of a scale that they already published. The dissemination and reliability of a scale with

1 *a wide focus is conditioned by the quality of the translation process into different*
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3 *languages. The large number of Chinese speakers around the world would increase*
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6 *the potential impact of this translation and this work may represent a major step*
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9 *towards a widespread use of the SECONDS.*
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11 *We think this is primordial to test the reliability and validity of the same scale in*
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13 *different languages. The French version was initially published, but our validation*
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16 *design is different from the French version. Indeed, we evaluated DoC patients in*
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19 *five sessions, which can more accurately reflect the diagnosis of patients and reduce*
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22 *the rate of misdiagnosis. Our results confirmed that SECONDS are shorter than*
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25 *CRS-R evaluations, but also that a reliable diagnosis could be attained with fewer*
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28 *assessments than with the CRS-R. Please see page 14 line 14-16.*
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36 **Comment:** Data confirming this seminal work is of course important and this new
37 study improves our understanding regarding the properties of the SECONDS. The
38 fact that the SECONDS seems to better detect a progression of UWS towards MCS
39 recovery as compared to the CRS-R is very interesting and highlights the role
40 of the item "pain anticipation".
41

42 ➤ **Reply:** *Thanks for your comment.*
43
44

45 **Comment:** Another important issue is related to the possibility of evolution in
46 terms of DoC diagnosis during the 2 weeks period of assessment. Indeed, we know
47 that the patient can improve especially during the sub-acute phase. This issue
48 should be more discussed given that 19 patients (10 TBI and 9 non-TBI) were
49 included before the delay of chronicity proposed by Giacino et al. guidelines
50 Neurology 2018 (3 months for non TBI and 12 months for TBI).
51

52 ➤ **Reply:** *We thank you for your relevant comment. Please find below a few*
53 *references to support our approach:*
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1 *-the term "chronic " is only recommended by the American guidelines and*
2 *defines an entirely stable clinical status, except in very rare cases[1],*
3 *attained after 3 or 12 months.*
4 *-the term "prolonged DoC (>28 days)" was also proposed by Giacino' s*
5 *guidelines in 2018 and adopted by all recent guidelines worldwide and*
6 *defines the threshold beyond the acute phase where the patient's status has*
7 *achieved some stability, therefore suitable to be included in diagnostic*
8 *studies like ours [2, 3]. Please note that we haven' t used the term*
9 *"chronic" in our manuscript, always "prolonged".*
10 *Additionally, any spontaneous evolution during the assessment window would*
11 *only have (falsely) decreased our test performance results (a patient*
12 *recovering would introduce apparent mismatch between assessments), without*
13 *risk to create false positive results.*
14 *- We have mentioned these aspects in Limitations Page 20 line 13-16.*

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21 **Comment:** The absence of the behaviour "functional use of object" in the SECONDS
22 is a limitation regarding the ability to diagnose emergence of MCS (EMCS) in
23 some patients (n=2 in this study). This issue should be more criticized and an
24 evolution of the scale adding this important behaviour for the diagnosis of
25 eMCS (particularly for patients with language disorder) should be asked.

26
27 ➤ **Reply:** *Thanks for your valuable advice. Please note that our aim is here to*
28 *formally translate and validate this existing scale, not to bring*
29 *modifications. That said, we agree that this should be discussed in our*
30 *manuscript.*

31
32 *- Please note that the items of SECONDS were selected based on CRS-R items*
33 *which were the most frequently observed in MCS patients[4].*
34 *- As notably discussed in Aubinet et al. 2021 (based on Giacino et al.*
35 *2002), "recovery from MCS to higher states of consciousness occurs along a*
36 *continuum in which the upper boundary is necessarily arbitrary".*
37 *Functional use of objects was chosen as a criterion of EMCS along with*
38 *functional communication because these behaviors are typically observed*
39 *during recovery, but object use highly depends on motor function and is*
40 *sometimes considered to require lower attentional resources than*
41 *communication. " [5, 6].*

42 *Some authors argue that the EMCS criteria should be changed and that*
43 *functional use of objects requires too low attentional resources to claim*
44 *EMCS[7]. Future research on this scale may one day lead to a revised or*
45 *modified version (which may include new items) if the evidence in this*
46 *direction is sufficient. Again, our results suggest that the mismatches*
47 *brought by the absence of this item are not a major issue in our cohort.*
48 *- We have added this point to the discussion. Please see Page 18 line 21.*

Minor considerations:

Comment: Page 3 : in the definition of MCS+ vs MCS-, the initial subcategorization was larger than only related to language signs of consciousness (Bruno et al. J Neurol 2011): "MCS+ describes high-level behavioural responses (i.e., command following, intelligible verbalizations or non-functional communication) and MCS- describes low-level behavioural responses (i.e., visual pursuit, localization of noxious stimulation or contingent behaviour such as appropriate smiling or crying to emotional stimuli)."

➤ **Reply:** *Thank for your comments. Please note that one can consider the examples given by the reviewer as "language-related signs of consciousness". For clarity, we have added in the manuscript some examples to be sure it would be clear for the readers too. Page 3 line 10-13.*

Comment: Page 7 line 9: "the degree off agreement ..." should be replaced by "the degree of agreement..."

➤ **Reply:** *We thank for your careful reading and it has been rectified.*

Comment: Page 13: in the following sentence line 42: "...the presentation (53%, P3, 16, 17...)..." I propose that the percentage should be placed previously in the sentence after "... 9 of these patients ..." idem in the following sentences.

➤ **Reply:** *Thanks for your comment and it has been adjusted.*

Comment:Page 13 lines 47 to 53 : I think the following sentence is incomplete because the given diagnosis with the SECONDS isn't clearly mentioned "the best SECONDS diagnosis of 1 patient (6%, P43) was consistent..."

➤ **Reply:** *Thanks for your comment and it has been updated at Page 13 lines 19 to 22.*

Reviewer #2: A. In brief

This manuscript is the transcription of an validated scale named SECONDS, used to assess disorders of consciousness (DoC) from French (original language) into Mandarin. The methodology is based on translation and back translation then validation of the Mandarin version by the methodology used in the original validation of the scale i.e. comparison between SECONDS and CRS-R (gold standard of DoC assessment). Concurrent validity, intra/ inter reliability have been evaluated and showed substancial validity and almost perfect reliability.

B. Main impressions

The topic is interesting. SECONDS is a useful tool in DoC assessment. It is useful to have translated versions available. This allows accurate evaluation

by the professionals, limits biases and avoid imprecisions. Considering the number of Mandarin speakers around the world, this translation and validation could have a great impact.

Comment: Why proposing a letter to the editor and not an original article?

➤ **Reply:** *The Editor suggested that we submit the manuscript in the form of a letter.*

C. Specific comments and suggestions

1. **Comment:** Does the abstract accurately reflect the content? The background paragraph doesn't say a word about SECONDS. Topic and objectives are not clearly defined.

➤ **Reply:** *We gratefully appreciate your valuable suggestion. We have modified the abstract accordingly.*

2. **Comment:** I suggest you could qualify some of your words when comparing CRS-R and SECONDS to present a more objective point of view:

- In the abstract, you emphasize the importance of repeated evaluations by CRS R but both CRS R and SECONDS require repeated passings

- Page 3 line 59: you seem to say that SECONDS doesn't require training. But Aubinet et al. (ref 13 you cited) write: "the SECONDS provides an easy-to-use assessment that requires [...] potentially a shorter training (given the low number of items) as compared with the CRS-R, whose reliability was shown to be influenced by raters' level of experience."

➤ **Reply:** *We gratefully thank for the precious time the Reviewer spent making constructive remarks. We agree that the correct administration of any behavioral scale requires some degree of training. Thanks to its lower number of items, shorter administration time and interactive training material[8], the SECONDS will likely require a much shorter training time than the CRS-R and other scales used to assess consciousness. We have rephrased the appropriate sections in the abstract and Page 4 line 2.*

3. **Comment:** Page 5, line 25. I would suggest using 'Mandarin' instead of 'Chinese' as elsewhere in the text.

➤ **Reply:** *Thanks for your suggestion. We have modified in the text.*

4. **Comment:** Page 6, line 9. I understand the impact on fatigue effect. But how did a break between each assessment impact fluctuation of vigilance?

➤ **Reply:** *We thank you for your comment. We have modified in Page 6, line 8-9.*

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5. **Comment:** Page 6. Discussion. The patients' group is heterogenous. This should have been discussed.

➤ *Reply: Thank you very much for your valuable advice. We have added this aspect in Page 20, line 13-16.*

6. **Comment:** Page 16. Discussion. Some points are missing in the discussion. There is no comparison with the result of the original validation article (French version, Aubinet et al. ref 13). Concurrent validity of the Mandarin version is lower than the one if the French version. Results are comparable for intra/inter reliability. Levels of disagreements between SECONDS and CRS-R are comparable in the original French version and the Mandarin one.

➤ *Reply: Thank you for pointing out this problem in manuscript. We have added these comparisons from Page 18, line 10-19.*

D. Detailed review

1. **Comment:** Page 3, line 45: the FOUR scale assess more coma than DoC.

➤ *Reply: Indeed, the FOUR scale is commonly used in the assessment of comatose patients in the intensive care unit (ICU), and we have replaced it with another clinical scale to assess DoC (SMART).*

2. **Comment:** Page 6, line 43: Is the order of the assessments always the same? Randomized?

➤ *Reply: Thanks for your comment, the order of the assessments was randomized. During session 1 the order of assessment of assessor A (and B and C) was also randomized. We have modified and emphasized it in Page 7, line 2.*

3. **Comment:** Page 16, line 45. Procedure: How many assessors in total? Is assessor A (and B and C) the same for each patient? From page 16 and additional materials, I assume they are not. Can you clarify this question in the text?

➤ *Reply: We had three assessors in total. And assessor A (and B and C) was the same for each patient. Assessor A did the assessment twice in session 1. In the article, A1 means the first assessment done by Assessor A, and A2 means the second one. We have clarified it in Page 16, line 3 and additional materials.*

4. **Comment:** Page 6, Figure 1 is very clear and helps understanding methodology

➤ *Reply: Thanks for your comment.*

5. **Comment:** Page 7, line 47. Including 2 patients at acute phase induces bias. The group would have been more homogeneous without these 2 patients. Do you assume their consciousness level stay stable during the procedure?

➤ *Reply: We greatly appreciate your advice. We excluded these 2 patients to*

1 *improve homogeneity. And we add two prolonged patients to replace them.*
2 *- We have discussed in Limitation, Page 20 line 13-17.*
3

4 6. **Comment:** Page 9, line 4. Time is expressed in days in the text and in months
5 in the Table 1. Is it possible to use the same unit?
6

7 ➤ *Reply: Thanks for your suggestion. We have unified these units.*
8

9
10 7. **Comment:** Page 10, line 11 and 44. In Table 1, what do asterisks mean?

11 ➤ *Reply: We are sorry for omitting the legend of asterisk, and asterisks*
12 *mean acute patient before, but now we have removed these two patients and*
13 *revised that under the Table.*
14
15

16 8. **Comment:** Page 13, line 47 to page 14, line 9. Could you show tables (as
17 Figure 2) to compare best CRS-R to session 1 SECONDS and best SECONDS to
18 session 1 CRS- R? This would clarify the data in the text.
19

20 ➤ *Reply: Thank you for your relevant suggestion. And we have added the*
21 *figure as Sup 2 in the supplementary material.*
22
23

24 9. **Comment:** Page 14, from line 34 to 39: This is not a result. Those lines
25 should be placed in the discussion section.
26

27 ➤ *Reply: Thank you so much for your careful check. We have modified it.*
28
29

30 10. **Comment:** Page 16. Why naming the assessors in a different way (from
31 Assessor A, B, C to Assessors 1, 2, 3)?
32

33 ➤ *Reply: Thanks for your careful reading. There are in fact no Assessors 1,*
34 *2, 3. We made the mistake of writing A1 for "Assessor 1". We have fixed*
35 *the error and elaborated A1 and A2 in page 16 and supplementary material.*
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38 11.

39 12. **Comment:** Page 17, lines 31 and 32. I don't think you can consider
40 differences when comparing best CRS-R to best SECONDS as "few differences". You
41 score those differences between 19 and 23%. Thank you for reconsidering the
42 sentence.
43

44 ➤ *Reply: Thank you for pointing out this problem in manuscript. We have*
45 *modified it.*
46
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48 13. **Comment:** Page 18, line 3 to 19. This sentence is not clear. I cannot
49 understand what you mean. Can you clarify?
50

51 ➤ *Reply: Thanks for your comment. We have modified the sentence.*
52
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54 14. **Comment:** Page 18, line 45. You didn't test it in ICU, so you cannot say it
55 is suitable. Thank you for replacing by 'it seems suitable'.
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57 ➤ *Reply: Thank you for this relevant suggestion. We have modified the sentence.*
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Mandarin Validation of the Simplified Evaluation of CONsciousness Disorders

(SECONDS)

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Key words: coma, disorder of consciousness, behavioral scale, rehabilitation, diagnosis

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number of additional materials : 1

Mandarin Validation of the Simplified Evaluation of CONsciousness Disorders

(SECONDS)

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CRS-R: Coma Recovery Scale-Revised

DoC: Disorder of Consciousness

EMCS: Emerge from the minimally conscious state

IQR: Interquartile Range

MCS-: Minimally Conscious State minus

MCS+: Minimally Conscious State plus

SMART: the Sensory Modality Assessment and Rehabilitation Technique

SECONDS: the Simplified Evaluation of CONsciousness Disorders

SD: Standard Deviation

TBI: Traumatic Brain Injury

UWS: Unresponsive Wakefulness Syndrome

WHIM: the Wessex Head Injury Matrix

1 **Dear Editor,**

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3 The pathogenesis of severe brain injury is complex, and advances in medical technology have
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5
6 increased the number of people who have survived severe brain injury in the past 50 years.
7
8
9 After the acute stage of cerebral injury, some people fully recover from coma, while others
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11 develop a disorder of consciousness (DoC) such as the unresponsive wakefulness syndrome
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13 (UWS) and the minimally conscious state (MCS). Persons in UWS are awake but not aware
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15 (without any reproducible sign of consciousness) , they only exhibit reflex behaviors (1).
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19 Persons in MCS are both awake and aware, they present reproducible and purposeful
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21 behaviors (2). MCS can be further divided based on the presence of language-related
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23 behaviors, into MCS “minus” (language-unrelated signs of consciousness, e.g., visual pursuit,
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25 localization of noxious stimulation or contingent behavior such as appropriate smiling or crying
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27 to emotional stimuli) and MCS “plus” (language-related signs of consciousness, i.e., command
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29 following, intelligible verbalizations or non-functional communication) categories (3). When
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31 persons recover functional communication and/or use of objects, they emerge from the
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34 minimally conscious state (EMCS) (2).
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44 An accurate diagnosis is crucial because it can influence the treatment of persons and potential
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46 end-of-life decisions (4). Several scales exist to evaluate the persons’ level of consciousness,
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48 e.g., the Coma Recovery Scale-Revised (CRS-R) (5), the Sensory Modality Assessment and
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50 Rehabilitation Technique (SMART) (6), or the Wessex Head Injury Matrix (WHIM) (7). Although
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52 the CRS-R is highly recommended as it has the highest test performances compared to other
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54 scales (8), it is time-demanding (median of 17 minutes) and requires a longer training (i.e.,
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more items to administer) (9). In addition, with the existence of high fluctuations in the person's level of consciousness, recent guidelines emphasize the importance of repeated evaluations (10, 11), which, consequently, increase even more the time clinicians need to dedicate for an accurate assessment of individuals with DoC.

Recently, the Simplified Evaluation of CONsciousness Disorders (SECONDS) (12, 13) was proposed as a new scale based on the most frequent items of the CRS-R that denote MCS (14). The SECONDS is faster to administer (median of 7 minutes) and easy-to-use. It could thus greatly benefit the care of DoC persons in clinical settings such as the intensive care units and reduce the risk of misdiagnosis. It includes 8 items (6 mandatory and 2 conditional) inspired from the most frequently observed signs of consciousness among DoC individuals when using the CRS-R.

The SECONDS has been validated in French participants (13). To promote accurate assessments of DoC individuals and the development of clinical research on DoC in China, we here propose and validate a version of the SECONDS translated into Mandarin (15). Hence, this study aims to assess the concurrent validity, intra-rater reliability, and inter-rater reliability of the Mandarin version of the SECONDS (15).

We first translated the French version of the SECONDS with the permission and assistance of the original authors (13). Then we recruited individuals at the Department of Consciousness Disorders in Shanghai Yongci Rehabilitation Hospital (Shanghai, China) from December 2021

1 to November 2022. The inclusion criteria were (1) Prolonged DoC (following severe acquired
2 brain injury, longer than 28 days); (2) Age: 18-85 years old; (3) No history of other neurological
3 or psychiatric deficits; (4) Ability to speak Mandarin fluently; and (5) Medical stability (e.g.,
4 absence of mechanical ventilation, sedation, infection).
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14 The ethics committee of the Shanghai Yongci Rehabilitation hospital and the Hangzhou Normal
15 University both approved this investigation. Informed consents were signed by the participant's
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19 legal representative.
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25 Overall, three distinct assessors who were experienced and trained to use the CRS-R,
26 assessed participants. All assessments were completed within two weeks (i.e., five CRS-R to
27
28 obtain a reliable diagnosis (16), and 7 SECONDS performed by 3 different assessors in the 2
29
30 weeks). Session 1 included one evaluation with the CRS-R performed by one assessor (i.e.,
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32 concurrent validity) and three evaluations with the SECONDS performed by two assessors (i.e.,
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34 intra-rater reliability and inter-rater reliability). The other sessions (2 to 5) each included one
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36 evaluation with the SECONDS and one evaluation with the CRS-R (i.e., concurrent validity)
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38 performed by two assessors. Each SECONDS was performed alternatively either before or
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40 after the CRS-R assessment. To avoid fatigue effects a break of 30 to 80 min between each
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42 assessment was taken. Until the end of the protocol, all three assessors were blinded to the
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44 scores acquired by the other assessors. Figure 1 illustrates the procedure.
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58 Descriptive statistics of participant's characteristics (e.g., age, time since brain injury) were
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1 calculated as mean (SD) and sex and etiology as percentages (%). Weighted Cohen's Kappa
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3 was used to calculate the degree of agreement, using a predefined table of weights that
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5 measures the degree of disagreement between the two raters, with higher weight indicating
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7 greater disagreement (17). Weighted Cohen's Kappa was used for three measures: 1)
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9 Concurrent validity (i.e., between same-day CRS-R and SECONDS diagnoses, and also
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11 between best SECONDS (best of all 7) and best CRS-R diagnoses), 2) intra-rater reliability
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13 (between the two assessments of assessor A on Session 1), and 3) inter-rater reliability
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15 (between the assessments of assessors A and C on Session 1). We also investigated
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17 concurrent validity using Spearman correlation.
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28 We enrolled 49 participants with DoC. Two participants dropped out of the trial due to
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30 complications that required a transfer to another hospital. Thus, 47 participants with prolonged
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32 DoC completed the study. The individual data of participants are shown in Table 1.
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39 The concurrent validity between diagnoses made with the CRS-R and the SECONDS on the
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41 same day was substantial (mean $K = 0.62$, $r_s = 0.74$, $p < 0.001$, when considering MCS- and
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43 MCS+; mean $K = 0.61$, $r_s = 0.67$, $p < 0.001$, when considering one single MCS category).
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50 The concurrent validity between the best CRS-R and the best SECONDS (best of all 7)
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52 was also substantial ($K = 0.69$, $r_s = 0.86$, when considering MCS- and MCS+; $K = 0.72$, $r_s =$
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54 0.84 , when considering one single MCS category).
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58 Figure 2 illustrates the details.
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1 When considering MCS- and MCS+ as separate categories (A1: 2 Coma, 25 UWS, 9 MCS-,
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3 10 MCS+, 1 EMCS; A2: 2 Coma, 22 UWS, 13 MCS-, 9 MCS+, 1 EMCS; A1: Assessor A first
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5 assessment in session 1. A2: Assessor A second assessment in session 1), the weighted
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7 kappa of two SECONDS assessments by the same assessor was 0.91 ($p < 0.001$), When
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9 considering one single MCS category (A1: 2 Coma, 25 UWS, 19 MCS, 1 EMCS; A2: 2
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11 Coma, 22 UWS, 22 MCS, 1 EMCS), the weighted kappa of two SECONDS assessments by
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13 the same assessor was 0.90 ($p < 0.001$) which demonstrates that the scale has an almost
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15 perfect intra-rater reliability with the same evaluator rating the same individual at different
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17 times of the same day.
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28 Inter-rater reliability for the SECONDS was substantial ($K = 0.75$, $p < 0.001$, when considering
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30 MCS- and MCS+ separately; $K = 0.76$, $p < 0.001$, when considering one single MCS
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32 category), which indicates that the SECONDS could reliably assess the same individual with
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34 multiple assessors.
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41 The supplementary material contains the specific data.
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47 We propose a standardized translation of the SECONDS tool into Mandarin, developed
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49 through a validated process by a collaboration between professional translators and experts
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51 in DoC, including both native French and Mandarin speakers. This validation study reveals
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53 that the translation of the SECONDS into Mandarin has a substantial concurrent validity
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55 compared to the CRS-R, an almost perfect intra-rater reliability and a substantial inter-rater
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1 reliability. This result is comparable to previous research (13) showing that the SECONDS is
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3 a reliable and valid scale to assess individuals with DoC.
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9 In our study, concurrent validity was substantial. The CRS-R is an internationally recognized
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11 bedside behavior assessment scale for DoC, while the SECONDS is a recently developed
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13 assessment tool. The two scales were compared and evaluated over two weeks, and some
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15 differences were observed in terms of diagnosis. Some mismatches observed between
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17 same-day exams were in fact linked to the “slower” ability of the CRS-R to identify the correct
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19 diagnosis on the first assessment, as revealed by subsequent CRS-R diagnoses that
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21 eventually matched the first SECONDS. It seems to indicate that the SECONDS provides an
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23 accurate diagnosis after fewer assessments compared to the CRS-R.
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33 Intra-rater reliability was almost perfect, which suggests that the results of the same
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35 evaluator are reliable. We found a reduced number of UWS diagnoses and an increase in
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37 the number of MCS-/MCS in the second assessment of assessor A in “Session 1”, which
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39 indicates that repeating SECONDS enhanced the rate of MCS- detection. This finding is in
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41 line with earlier research that suggests to repeat assessments (16).
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50 Furthermore, inter-rater reliability was substantial, which means that the accuracy of the
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52 diagnosis can be promise even if the person is assessed by multiple evaluators. When we
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54 considered five categories, due to the fluctuation of participants' consciousness state or
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56 cooperation degree between participants and assessors and the difference of command
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choice among different evaluators, we found differences in participants' diagnoses between these two types (MCS-/MCS+).

The SECONDS features only one of the two items warranting EMCS in the CRS-R, functional communication. Significantly, some authors have highlighted that the criteria of EMCS constitute an upper boundary to DoC that must be set arbitrarily. Since “functional use of objects” depends highly on motor function and potentially requires lower attentional resources than communication, its relevance as emergence criterion was previously questioned (18) . Future research on the SECONDS may one day add this item if the evidence in this direction is sufficient.

Overall, the diagnostic changes of participants in SECONDS and CRS-R within five days show that the SECONDS has an excellent detection rate to diagnose MCS, particularly for MCS+, which is mostly due to the item of pain anticipation, which makes good use of the capacity of the human body's self-protection (19).

Future studies should replicate these results on larger sample sizes, which would allow subgroup analyses and better understanding of the SECONDS test properties. In particular, all of the participants were in prolonged DoC (>28 days), which calls for subsequent studies validating this tool among participants in the acute phase. In addition, neuroimaging and electrophysiological measures were not included in this study, therefore, there is a risk that this study may include some participants with covert consciousness that has not been

1 detected at the bedside (20). Several multimodal assessments could be further carried out to
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3 examine the misdiagnosis rate of bedside assessments when using the SECONDS.
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9 In conclusion, our study demonstrates that the Mandarin version of the SECONDS has
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11 almost perfect reliability and substantial validity. This version could be used to promote the
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13 widespread use of standardized and validated bedside diagnostic tools for people with DoC
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15 in a broad array of clinical settings throughout China, and therefore reduce misdiagnosis
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17 rates.
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25 The difference between the validation results of the Mandarin and French version and the
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27 limitations of this study are in the supplementary material.
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3 the Mind-Care foundation. LS is research fellow, OG and AT are research associates, and
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6 SL is research director at FRS-FNRS.
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11 The authors declare that there is no conflict of interest regarding the publication of this paper.
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17 This study is prospective and has been registered in the Clinical Trials.gov, the number is
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Figure 1. Description of the procedure of the SECONDS validation. Each SECONDS was performed alternatively before or after a CRS-R assessment, the order of the assessments was randomized (i.e., five CRS-R to obtain a reliable diagnosis and 7 SECONDS performed by 3 different assessors in the 2 weeks) in five different sessions. Assessor A administered the SECONDS twice in “Session 1”; on “Session 2-5” Assessor A administered the SECONDS or CRS-R once a day; Assessor A and Assessor B evaluated participants by using CRS-R and SECONDS alternately randomized for the order between CRS-R and SECONDS each day; Assessor C administered the SECONDS once on “Session 1”. There were only three assessors throughout the trial and assessor A (and B and C) was the same for each participant.

Figure 2. Diagnostic agreement between the SECONDS and the CRS-R. The diagnosis made with the SECONDS and the CRS-R during Session 1 are illustrated on the left. The diagnosis of the best SECONDS and the best CRS-R are illustrated on the right. The numbers on the diagonal indicate the number of participants with matching diagnosis using the SECONDS and the CRS-R. Color boxes off the diagonal show diagnostic discrepancies between the two scales. Yellow boxes show a better diagnosis in the SECONDS compared to CRS-R. Blue show a better diagnosis for the CRS-R compared to the SECONDS. a. Results when considering MCS- and MCS+ separately b. Results when considering MCS as one single category.

For Session 1, we found a discrepancy in the diagnosis between the CRS-R and the SECONDS in 17 (36%) participants: 13 participants had a better diagnosis with the SECONDS, and 4 participants had a better diagnosis with the CRS-R. When we compared the diagnosis made during Session 1 for these 17 participants with the best diagnosis made across all Sessions, we found that for 9 of these participants (53%, P3, 16, 17, 22, 24, 27, 41, 42, 47), whose mismatch indicated a better diagnosis using the SECONDS, the SECONDS diagnosis (made during Session 1) was actually matching the best diagnosis made with the CRS-R, obtained in a subsequent Session, only after multiple CRS-R evaluations. The best SECONDS diagnosis of 1 participant (6%, P43, MCS-) was consistent with the diagnosis of CRS-R in Session 1 and best diagnosis of CRS-R, after repeated assessments. The best SECONDS diagnosis of 1 participant (6%, P19, MCS+) was better than diagnosis of CRS-R in Session 1 (MCS-) and best diagnosis of CRS-R (MCS-), after

1 repeated assessments. Only 6 participants (35%, P7, 18, 35, 37, 39, 40) with a mismatch
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3 had a stable diagnosis, no matter in Session 1 or after repeated assessments (see Sup 2 in
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5 the supplementary materials). Four participants (P18, 35, 39, 40) had a better diagnosis with
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7 the SECONDS, and two participants (P7, 37) had a better diagnosis with the CRS-R. Three
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9 of these six (50%, P18, 35, 39) participants had a better diagnosis with the SECONDS than
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11 the CRS-R because of the pain anticipation item.
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19 Looking at the best diagnosis made with the CRS-R and the SECONDS, two participants
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21 were diagnosed EMCS with the CRS-R because they showed functional use of objects,
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23 whereas they were diagnosed MCS+ in the SECONDS because this behavior does not exist
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25 in the SECONDS (P7, P33). Five participants were diagnosed MCS+ in the SECONDS due to
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27 pain anticipation item, while they were diagnosed MCS- with the CRS-R (P18, 19, 35, 39,
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29 40). We had one participant (P23) whose diagnosis was EMCS when answering situational
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31 questions with the SECONDS, but MCS+ when answering visual and auditory questions with
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33 the CRS-R. When we only considered the same diagnosis (n=33) made with best SECONDS
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35 and best CRS-R, we found that all participants received the best diagnosis with SECONDS
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37 earlier than (n=11) or at the same time as (n=22) with CRS-R (see Table 1).
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50 We then considered only one single MCS category, combining MCS- and MCS+ together, to
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52 observe if SECONDS has a better awareness detection rate. For Session 1, we found a
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54 discrepancy in the diagnosis between the CRS-R and the SECONDS in 11 (23%)
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56 participants. These 11 participants (P7, 16, 17, 19, 22, 24, 37, 40, 41, 43, 47) had the same
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condition as described above. Compared to the 17 participants mentioned above, there are 6 participants fewer (P3, 18, 27, 35, 39, 42), due to the pain anticipation item which qualified all of these 6 participants for MCS+ diagnosis when using the SECONDS. As noticed before, the best CRS-R diagnosis (after repeated assessments) was consistent with the diagnosis of the SECONDS in Session 1 among 3 of these 6 participants (50%, P3, 27, 42).

Table 1. Individual demographic and diagnosis data

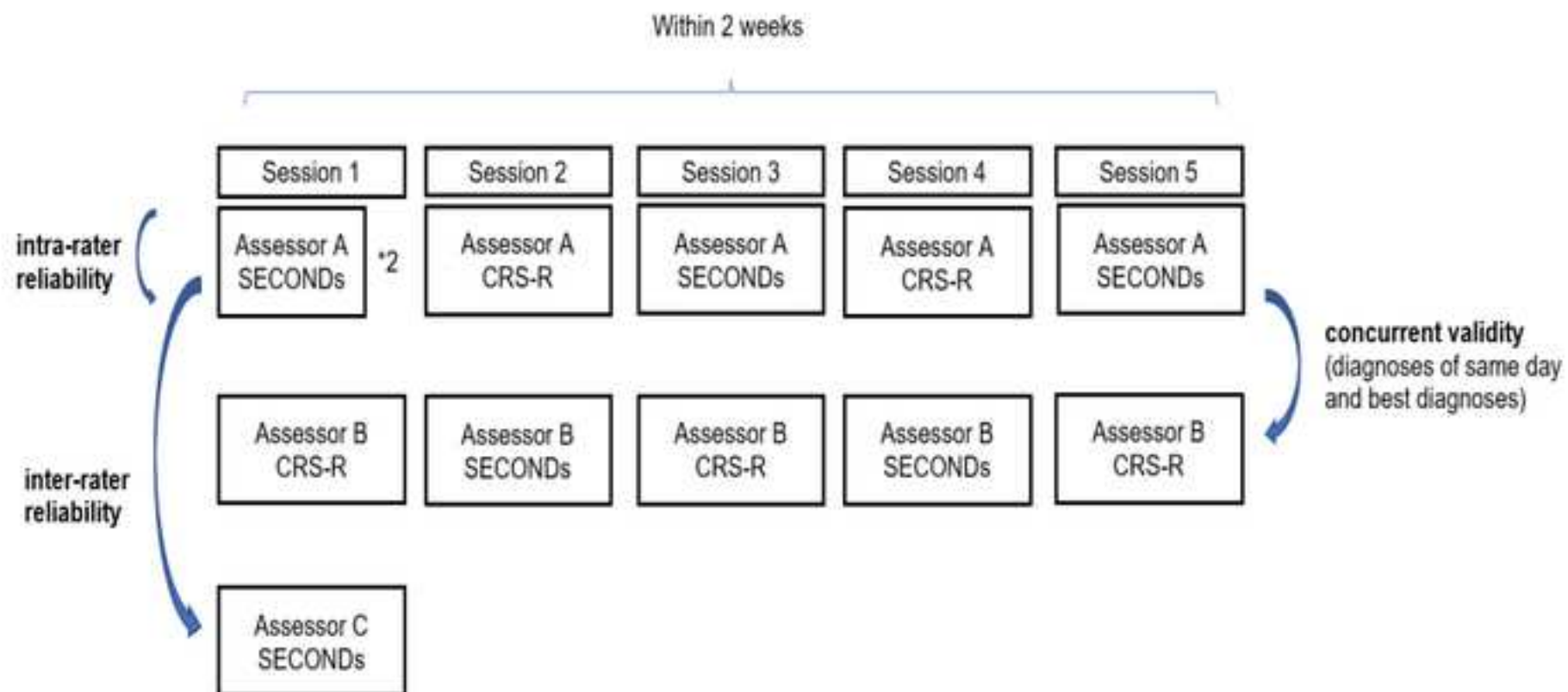
Participants	Age	Gender	Etiology	Time since injury (months)	Best CRS-R	Best SECONDS
1	51	F	TBI	11.87	MCS ⁻³	MCS ⁻¹
2	75	F	hemorrhagic stroke	8.33	MCS ⁻²	UWS ¹
3	47	F	anoxia	11.50	MCS ⁺²	MCS ⁺¹
4	60	F	hemorrhagic stroke	2.30	UWS ¹	UWS ¹
5	71	M	anoxia	25.90	UWS ¹	UWS ¹
6	69	M	hemorrhagic stroke	4.37	MCS ⁻¹	MCS ⁻¹
7	25	M	TBI	13.03	EMCS ¹	MCS ⁺¹
8	39	M	anoxia	1.00	UWS ¹	UWS ¹
9	65	M	TBI	20.77	UWS ¹	UWS ¹
10	75	M	anoxia	>24	MCS ⁻¹	MCS ⁻¹
11	36	M	hemorrhagic stroke	15.33	UWS ¹	UWS ¹
12	41	F	anoxia	15.80	UWS ¹	UWS ¹
13	37	M	hemorrhagic stroke	9.90	UWS ¹	UWS ¹
14	81	M	anoxia	15.77	MCS ⁻⁴	UWS ¹
15	44	M	anoxia	35.87	MCS ⁻¹	MCS ⁻¹
16	29	M	TBI	9.57	MCS ⁻²	MCS ⁻¹
17	71	M	anoxia	11.23	MCS ⁻²	MCS ⁻¹
18	66	M	TBI	10.67	MCS ⁻¹	MCS ⁺¹
19	71	M	anoxia	9.63	MCS ⁻¹	MCS ⁺³

20	43	M	hemorrhagic stroke	2.20	Coma ¹	UWS ³
21	71	M	TBI	9.93	UWS ¹	UWS ¹
22	27	F	hemorrhagic stroke	1.70	MCS ⁻³	MCS ⁻¹
23	40	M	hemorrhagic stroke	25.07	MCS ⁺¹	EMCS ²
24	43	M	hemorrhagic stroke	4.37	MCS ⁻²	MCS ⁻¹
25	57	F	TBI	1.93	UWS ¹	UWS ¹
26	22	F	anoxia	20.43	MCS ⁻¹	MCS ⁻¹
27	66	M	TBI	1.87	MCS ⁺³	MCS ⁺¹
28	63	F	hemorrhagic stroke	2.43	MCS ⁻¹	MCS ⁻¹
29	43	M	anoxia	1.17	UWS ¹	UWS ¹
30	66	M	anoxia	29.87	UWS ¹	UWS ¹
31	49	M	anoxia	8.33	MCS ⁻⁴	MCS ⁻¹
32	52	M	hemorrhagic stroke	2.87	UWS ¹	UWS ¹
33	35	M	TBI	2.57	EMCS ²	MCS ⁺¹
34	33	M	hemorrhagic stroke	3.70	UWS ¹	UWS ¹
35	60	M	hemorrhagic stroke	5.13	MCS ⁻¹	MCS ⁺¹
36	65	M	anoxia	7.70	MCS ⁻⁵	UWS ¹
37	55	M	TBI	1.63	UWS ¹	Coma ¹
38	39	M	anoxia	10.90	MCS ⁻¹	MCS ⁺¹
39	51	M	hemorrhagic stroke	4.97	MCS ⁻¹	MCS ⁺¹
40	64	M	hemorrhagic stroke	3.07	MCS ⁻²	MCS ⁺¹
41	69	F	TBI	3.83	MCS ⁻²	MCS ⁻¹

42	56	M	hemorrhagic stroke	6.30	MCS+ ⁵	MCS+ ¹
43	44	M	TBI	17.50	MCS- ¹	MCS- ¹
44	57	M	anoxia	3.90	UWS ¹	UWS ¹
45	63	M	TBI	1.10	EMCS ¹	EMCS ¹
46	51	M	hemorrhagic stroke	4.23	MCS- ³	MCS- ³
47	47	M	hemorrhagic stroke	7.93	MCS- ²	MCS- ¹

There were 10 (21%) females, with 13 (28%) participants suffering from a traumatic brain injury (TBI), 18 (38%) from a hemorrhage stroke, and 16 (34%) from an anoxic brain injury. The mean age was 52 (15) (rang 22 to 81). The median time since brain injury time was 7.93 months, (interquartile range [IQR] 2.87-13.03, range 1 - 35.87). Numbers in superscript indicate which assessment allows the diagnosis: ¹ diagnosed by the first assessment; ² diagnosed by the second assessment; ³ diagnosed by the third assessment; ⁴ diagnosed by the fourth assessment; ⁵ diagnosed by the fifth assessment. Eleven participants (34%, P1, 3, 16, 17, 22, 24, 27, 31, 41, 42, 47) received the diagnosis on SECONDS earlier than CRS-R.

EMCS: Emerge from the minimally conscious state. F: female. M: male. MCS-: Minimally Conscious State minus. MCS+: Minimally Conscious State plus. TBI: Traumatic Brain Injury. UWS: Unresponsive Wakefulness Syndrome.



		Session 1 CRS-R					Best CRS-R					
		Coma	UWS	MCS-	MCS+	EMCS	Coma	UWS	MCS-	MCS+	EMCS	
Session 1 SECONDS	Coma	1	1	0	0	0	0	1	0	0	0	Best SECONDS
	UWS	0	20	2	0	0	1	14	3	0	0	
	MCS-	0	7	6	0	0	0	0	15	0	0	
	MCS+	0	0	6	2	1	0	0	6	3	2	
	EMCS	0	0	0	0	1	0	0	0	1	1	

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		Session 1 CRS-R				Best CRS-R				
		Coma	UWS	MCS	EMCS	Coma	UWS	MCS	EMCS	
Session 1 SECONDS	Coma	1	1	0	0	0	1	0	0	Best SECONDS
	UWS	0	20	2	0	1	14	3	0	
	MCS	0	7	14	1	0	0	24	2	
	EMCS	0	0	0	1	0	0	1	1	

b

