



The nociception coma scale: A new tool to assess nociception in disorders of consciousness

Caroline Schnakers^{a,*}, Camille Chatelle^a, Audrey Vanhauzenhuysse^a, Steve Majerus^{b,e}, Didier Ledoux^c, Melanie Boly^{a,d,e}, Marie-Aur lie Bruno^{a,e}, Pierre Boveroux^{a,f}, Athena Demertzi^a, Gustave Moonen^d, Steven Laureys^{a,d,e}

^a Coma Science Group, Cyclotron Research Centre, University of Li ge, Sart Tilman, B30, 4000 Li ge, Belgium

^b Department of Cognitive Sciences, University of Li ge, Li ge, Belgium

^c Department of Intensive Care, Centre Hospitalier Universitaire Sart Tilman, Li ge, Belgium

^d Department of Neurology, Centre Hospitalier Universitaire Sart Tilman, Sart Tilman, B30, 4000 Li ge, Belgium

^e Fund for Scientific Research – FNRS, Belgium

^f Department of Anesthesia, CHU Sart Tilman Hospital, University of Li ge, Li ge, Belgium

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ABSTRACT

Assessing behavioral responses to nociception is difficult in severely brain-injured patients recovering from coma. We here propose a new scale developed for assessing nociception in vegetative (VS) and minimally conscious (MCS) coma survivors, the Nociception Coma Scale (NCS), and explore its concurrent validity, inter-rater agreement and sensitivity. Concurrent validity was assessed by analyzing behavioral responses of 48 post-comatose patients to a noxious stimulation (pressure applied to the fingernail) (28 VS and 20 MCS; age range 20–82 years; 17 of traumatic etiology). Patients were assessed using the NCS and four other scales employed in non-communicative patients: the ‘Neonatal Infant Pain Scale’ (NIPS) and the ‘Faces, Legs, Activity, Cry, Consolability’ (FLACC) used in newborns; and the ‘Pain Assessment In Advanced Dementia Scale’ (PAINAD) and the ‘Checklist of Non-verbal Pain Indicators’ (CNPI) used in dementia. For the establishment of inter-rater agreement, fifteen patients were concurrently assessed by two examiners. Concurrent validity, assessed by Spearman rank order correlations between the NCS and the four other validated scales, was good. Cohen’s kappa analyses revealed a good to excellent inter-rater agreement for the NCS total and subscore measures, indicating that the scale yields reproducible findings across examiners. Finally, a significant difference between NCS total scores was observed as a function of diagnosis (i.e., VS or MCS). The NCS constitutes a sensitive clinical tool for assessing nociception in severely brain-injured patients. This scale constitutes the first step to a better management of patients recovering from coma.

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1. Introduction

Assessing nociception in severely brain-injured patients with disorders of consciousness represents a real challenge [20]. According to the International Association of Pain, “Pain is defined as an unpleasant sensory and emotional experience associated with real or potential tissue damage, or described in terms of such damage” [12]. Pain is hence a subjective first-person experience which has to be verbally or non-verbally reported to be accurately assessed. Nevertheless, self-reports are not possible to obtain in non-communicative patients, such as patients recovering from coma. For this reason, we will talk about nociception and not pain in this arti-

cle; nociception being defined as “an actually or potentially tissue damaging event transduced and encoded by nociceptors” [17].

Progress in intensive care has led to an increase in the number of patients who survive severe acute brain injury. These patients often pass through different altered states of consciousness before fully recovering awareness and, possibly, functional communication [18]. Patients in a vegetative state (VS) present no language production or comprehension [25] whereas patients in a minimally conscious state (MCS) may show reproducible but minimal and fluctuating signs of consciousness [7]. Neither VS nor MCS patients are able to reliably communicate a possible nociception by either verbal or non-verbal reports. At the same time, previous studies have shown that, contrary to VS patients [14], MCS patients may show a brain activation profile in response to noxious stimulation similar to healthy controls, suggesting a potential nociception [1,2] even if those cannot be expressed by the patient’s self-report.

* Corresponding author. Tel.: +32 4 366 23 62; fax: +32 4 366 29 46.

E-mail addresses: C.Schnakers@ulg.ac.be (C. Schnakers), steven.laureys@ulg.ac.be (S. Laureys).

Hence, detecting behavioral signs of nociception in patients recovering from coma hence represents an important medical and ethical challenge.

Numerous standardized behavioral scales have been developed to help the detection of subtle signs of consciousness [15,18]. Up to now, however, no scale has been specifically developed to assess nociception in VS and MCS patients [20]. To date, the presence or absence of nociception is inferred via motor responses following noxious stimulation, such as stereotypical responses, flexion withdrawal and localization responses [20]. These responses are commonly respectively linked to brainstem, subcortical or cortical activity [22]. Localization to noxious stimulation is the only motor response considered as indicative of conscious perception [7]. Specifying the degree of nociception or its saliency to the person is not feasible by only considering these responses.

Several scales have been developed and validated to detect signs of nociception in non-communicative patients, such as in newborns [16,19] or in the demented elderly [5,27]. These scales are based on behavioral observations and often take into account facial expressions, verbalizations/vocalizations, body movements or changes in emotional status (e.g., cries) [11,24]. However, no scale has been specifically adapted for assessing nociception in patients recovering from coma.

In this context, the aim of this article is to explore concurrent validity, inter-rater agreement and sensitivity of a new scale that we developed for assessing nociception in severely brain-injured patients, the Nociception Coma Scale, with comparison to four other scales used for newborns or elderly.

2. Methods

2.1. Participants

This study is a prospective multi-centric study with patients recruited from the acute care, neurology, neurorehabilitation and nursing home centers which are part of the Belgian federal network for vegetative and minimally conscious states. Inclusion criteria were (1) age ≥ 18 years, (2) no administration of neuromuscular function blockers and no sedation within the 24 h of enrollment, (3) the presence of periods of eye opening (indicating preserved sleep-wake cycles), (4) a diagnosis of vegetative state (VS) or minimally conscious state (MCS), based on the behavioral assessment performed using the Coma Recovery Scale-Revised (see below) [6]. Exclusion criteria were (1) documented history of prior brain injury, (2) premorbid history of developmental, psychiatric or neurologic illness resulting in documented functional disability up to time of the injury, (3) superior limb contusions, fractures or paralysis. The study was approved by the Ethics Committee of the Faculty of Medicine of the University of Liège and written informed consent was obtained by the patients' legal representative.

2.2. Procedure

(1) Concurrent validity: Five behavioral scales were administered in randomized order by an experienced neuropsychologist (CS) to assess patients' responses to noxious stimulation: the Neonatal Infant Pain Scale (NIPS), the Faces, Legs, Activity, Cry, Consolability pain assessment tool (FLACC), the Pain Assessment In Advanced Dementia Scale (PAINAD), the Checklist of Non-verbal Pain Indicators (CNPI) and the Nociception Coma Scale (NCS). The NIPS assesses facial expression, arm and leg movements, crying, breathing pattern and state of arousal and is scored from 0 (no nociception) to 7 (severe nociception); a score superior to 3 is suggesting nociception [16]. The FLACC assesses face, legs and general body movements, crying and consolability and is scored from 0 to 10 (se-

vere nociception) [19]. The PAINAD assesses breathing, negative vocalization, facial expression, body movements and consolability and is scored from 0 (no nociception) to 10 [27]. The CNPI assesses verbal complaints, vocalizations, facial expression, agitation and localization to noxious stimulation and is scored from 0 to 6 – a score of 1–2 suggesting light nociception, 3–4 moderate nociception and 5–6 severe nociception [5]. The NCS was developed according to behaviors generally considered during assessment of non-communicative patients, such as facial expression, changes in mental status (i.e., cries), vocalizations/verbalizations or body movements [11,24]. In a pilot study, we also assessed breathing responses but later discarded this item because of the difficulty to assess this behavior in patients not benefiting from respiratory monitoring devices [4]. Previous studies have also shown that autonomic changes, such as respiration and heart rate are no reliable indicators of nociception [3,9]. Other behaviors linked to nociception, such as changes in interpersonal interaction (e.g., decreased social interactions) and changes in routine activities (e.g., appetite and sleep changes) are not assessed by the NCS. Indeed, the inclusion of these behaviors is not appropriate as patients recovering from coma have few interpersonal interaction and activities. Additionally, the assessment of these behaviors requires relatively long periods of observation and may be biased by other factors, such as anxiety or depression. The proposed NCS assesses motor, verbal, visual and facial responses. Its total score ranges from 0 to 12 (Table 1; Complementary online material).

In order to ensure a sufficient level of arousal, each behavioral scale was administered while patients showed spontaneous eye opening. Two noxious stimulations were administered before completing the behavioral scales. Upper extremities were extended (as far as possible for spastic patients) and noxious stimulation consisted of applying pressure on the fingernail bed [23] of the middle finger of the left and then of the right hand using a Newton-meter (Force Dial, FDN 200 model; Connecticut, USA; www.wagnerinstruments.com). The Newton-meter allows the examiner to gauge the amount of pressure and hence allowed controlling the intensity of the noxious stimulation applied to the patient. Fingernail pressure was administered for a minimum of 5 s [6] and was stopped as soon as a behavioral response was observed. Behavioral responses were recorded for 10 s [6] after each noxious stimulus. Patients' consciousness level was assessed by using the Coma Recovery Scale-Revised (CRS-R) [6]. The CRS-R consists of 23 hierarchically arranged items that comprise six subscales addressing

Table 1

Protocol of the Nociception Coma Scale (detailed administration guidelines in Complementary online material).

<i>Motor response</i>
3 – Localization to noxious stimulation
2 – Flexion withdrawal
1 – Abnormal posturing
0 – None/flaccid
<i>Verbal response</i>
3 – Verbalisation (intelligible)
2 – Vocalisation
1 – Groaning
0 – None
<i>Visual response</i>
3 – Fixation
2 – Eyes movements
1 – Startle
0 – None
<i>Facial expression</i>
3 – Cry
2 – Grimace
1 – Oral reflexive movement/startle response
0 – None

arousal, auditory, visual, motor, oromotor/verbal and communication functions. The lowest item on each subscale represents reflexive activity while the highest item represents cognitively-mediated behaviors [6].

The concurrent validity was determined by comparing NCS total scores and subscores to the other scales (NIPS, FLACC, PAINAD and CNPI) by means of Spearman rank correlations.

(2) Inter-rater agreement: Fifteen patients (age range: 20–82 years; 8 females; 4 traumatic cases; 6 chronic cases) were assessed by two experienced neuropsychologists (CS and AV) during a single session in order to decrease the probability to observe inter-rater disagreement due to vigilance and/or consciousness fluctuations of the patient. Each examiner administered one of the two noxious stimulations.

To investigate the inter-rater agreement, Cohen's kappa (K) tests determined the reproducibility of NCS total scores and subscores between the different raters. K values of 0.4 or less were considered poor, values between 0.4 and 0.6 were considered fair to moderate, values between 0.6 and 0.8 were considered as good inter-observer agreement and values greater than 0.8 suggested excellent agreements [13].

(3) Assessment of sensitivity: the capacity of the NCS and of the other four scales (i.e., the NIPS, the FLACC, the PAINAD and the CNPI) to differentiate between the behavioral pattern of each diagnostic category (i.e., VS vs. MCS) in response to noxious stimulation was assessed by performing a t -test on each scale's total scores as a function of the diagnosis.

3. Results

We included 48 patients of whom 28 were vegetative and 20 minimally conscious according to the behavioral assessment performed using the Coma Recovery Scale-Revised [6] (age range 20–82 years; 28 females). Etiology was traumatic ($n = 17$), post-anoxic ($n = 10$), encephalitis ($n = 7$), ischemic stroke ($n = 7$) and intracerebral hemorrhage ($n = 7$). Thirty-one patients were assessed in the acute stage (i.e., <1 month post-injury) and 17 in the chronic stage (interval ranging from 1 month to 6 years). The amount of pressure that was applied (range 41–85 N/cm²) was not different according to the diagnosis (VS versus MCS) ($t(46) = .53$; $p = .60$). Time needed for NCS administrations varied between 1 and 5 min.

3.1. Concurrent validity

Total NCS scores showed significant correlations with total scores of NIPS, FLACC, PAINAD and CNPI. Verbal, visual and facial expression subscores of the NCS also showed significant correlation with all four scales. The motor subscores were significantly correlated to the PAINAD (Table 2).

3.2. Inter-rater agreement

Inter-rater agreement for the NCS total score was good ($K = .61$). For the different subscales, mean kappa values were good to excel-

lent (i.e., motor ($K = .93$), verbal ($K = .93$), visual ($K = .73$) and facial expression ($K = .73$) subscales).

3.3. Sensitivity

A significant difference ($t(46) = 3.86$; $p < .0005$) between NCS scores was obtained as a function of diagnosis (i.e., VS versus MCS). The NCS total score obtained in MCS patients (5.6 ± 2.1 ; range: 2–10) was higher than in VS patients (3.4 ± 1.8 ; range: 0–6) (Fig. 1). No differences according to level of consciousness were observed for the NIPS ($t(46) = 1.36$; $p = .18$), the FLACC ($t(46) = 1.61$; $p = .11$) or the PAINAD ($t(46) = 1.86$; $p = .07$) but the CNPI ($t(46) = 2.61$; $p = .01$) showed different total scores in VS (0.5 ± 0.5) as compared to MCS (1.1 ± 0.9).

In order to establish a relationship between NCS total scores and nociception intensity, we made additional analyses. Given that thresholds were previously determined for CNPI total scores [5], we performed an ANOVA on NCS total scores as a function of CNPI thresholds. Usually, a CNPI score of 0 suggests no nociception whereas a score of 1 or 2 suggests light nociception, a score of 3 or 4 moderate nociception and a score of 5 or 6 severe nociception. A significant difference was observed among NCS total scores according to CNPI thresholds, such as no nociception (2.5 ± 1.5), light nociception (5.1 ± 1.7) and moderate nociception (8.0 ± 1.0) (Fig. 2); severe nociception could not be assessed as none of the studied patients obtained a CNPI total score of 5 or 6.

Finally, no significant differences in NCS total scores were observed either as a function of the etiology ($F = .29$; $p = .98$) or the interval between assessment and brain insult (i.e., acute vs. chronic) ($t(46) = .60$; $p = .55$).

4. Discussion

The aim of this study was to investigate concurrent validity, inter-rater agreement and sensitivity of the Nociception Coma Scale, a new scale developed for assessing nociception in non-communicative patients recovering from coma (i.e., in VS and MCS patients). We obtained a good concurrent validity between the NCS and the four other validated scales suggesting that the NCS measures nociception similarly to the NIPS, the FLACC, the PAINAD and the CNPI. The highest correlation was observed between the NCS and the CNPI. All behaviors assessed by the CNPI (i.e., verbal complaints, vocalizations, facial expression, agitation and localization to noxious stimulation) are also assessed by the NCS. As regards NCS

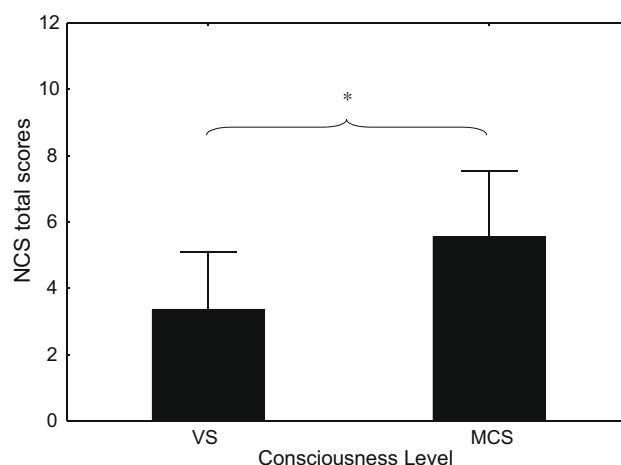


Fig. 1. Mean (and standard deviation) of NCS scores according to consciousness level (i.e., vegetative state – VS or minimally conscious state – MCS). Asterisk denotes a significant difference between consciousness level ($p < .0005$).

Table 2

Correlation coefficients between NCS total (sub)scores and total scores in four other scales (i.e., the NIPS, the FLACC, the CNPI and the PAINAD).

NCS	NIPS	FLACC	CNPI	PAINAD
Total scores	.71*	.69*	.80*	.72*
Motor subscores	.26	.26	.25	.30*
Verbal subscores	.42*	.52*	.52*	.44*
Visual subscores	.49*	.30*	.56*	.36*
Facial expression subscores	.66*	.74*	.74*	.79*

* $P < .05$.

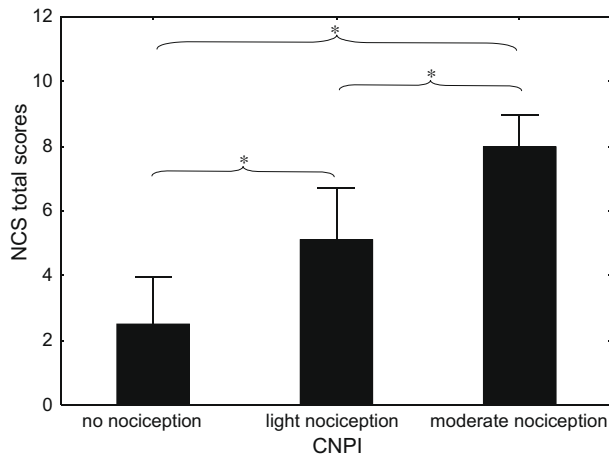


Fig. 2. Mean (and standard deviation) of Nociception Coma Scale (NCS) scores according to the Checklist of Non-verbal Pain Indicators (CNPI) [5] thresholds (i.e., no nociception, light nociception and moderate nociception). Asterisk marks significant difference between thresholds ($p < .05$).

subscores, verbal, visual and facial subscales were correlated to at least one scale suggesting that each of these NCS subscales assesses nociception. Inter-rater agreement for the NCS total score was good indicating that the scale yields reproducible findings across examiners. We also found good to excellent inter-rater agreement for each subscale. One could argue that the difference in the number of acute and chronic patients could bias our results. However, we did not find any difference in NCS total scores between acute and chronic patients suggesting that the time elapsed since the injury does not have an influence on the NCS total score. Concurrent validity and reliability was also comparable when analyzing given the 31 patients assessed in the acute stage (less than 1 month post-injury) and the 17 patients assessed in the chronic stage (with an interval ranging from one month to six years). Finally, NCS total scores were higher in MCS than in VS patients suggesting that our scale is adapted to assess nociception in patients with disorders of consciousness. Our results can be linked to previous functional neuroimaging studies showing a difference in brain activation between VS and MCS patients following noxious stimulation. Indeed, in VS patients, noxious stimulation only activates brainstem, thalamus and primary somatosensory cortex – the latter being functionally disconnected from the rest of the pain matrix encompassing secondary somatosensory, insular, anterior cingulate, parietal, premotor, and prefrontal cortices. The residual primary cortex activation in VS is therefore suggested to be isolated from higher-order associative cortical activity considered to be crucial in the conscious perception of the stimuli as well as from areas involved in the affective and cognitive processing of pain [14]. On the contrary, MCS patients were shown to have a brain activation following noxious stimulation very similar to that measured in healthy volunteers. The cortical integration observed in these patients is considered to possibly reflect nociception [2]. Moreover, MCS patients showed preserved activation of anterior cingulate cortex, suggesting preserved perception of stimulus unpleasantness [26]. It is therefore not surprising that the present behavioral study identified higher NCS total scores in MCS as compared to VS patients when Newton-meter intensity matched noxious stimuli were applied.

With the exception of the CNPI, the other scales, validated for newborns (i.e., the NIPS and the FLACC) or for people with dementia (i.e., the PAINAD and the CNPI) did not distinguish between VS and MCS patients suggesting that these scales are not adapted to assess nociception in patients with disorders of consciousness. Furthermore, as compared to the CNPI scores, the NCS scores, showed

wider ranges of subscores (e.g., a CNPI score of 0 corresponded to NCS scores between 0 and 5) suggesting that the NCS is more sensitive to detect different behavioral signs of nociception in VS and MCS. According to our results, the NCS represents a sensitive tool adapted for assessing nociception in severely brain-injured patients with disorders of consciousness.

Here, our objective was to develop a validated scale which could be used by clinicians even in case of short hospitalization periods and which could detect and monitor nociception in a standardized manner. An inadequate use of the NCS could be to use it in order to decide who is conscious or not and, therefore, who can receive treatment or not. First, the NCS is not a scale aiming to disentangle VS from MCS patients; others scales have been developed for this purpose [6]. Second, according to us and considering the levels of clinical uncertainty, pain treatment should be considered in all VS or MCS patients [20]. The real clinical interest of the NCS is to monitor patients in presence of a potential noxious stimulation (e.g., decubitus ulcers) and to give to the clinician a standardized but also adapted tool they can use for objectively detecting, communicating and following of non-communicative patient's behaviors and their daily management [4,20,21]. The use of the NCS will hence allow monitoring treatment in order to avoid sedative effects as well as under-uses of analgesics [21].

The NCS also offers a tool which, for research purposes, permits to better define behavioral signs of nociception and their correlation with functional neuroimaging data. Indeed, clinical signs (e.g., grimaces) are often considered as behavioral signs of nociception in the assessment of non-communicative patients [10,11,24]. However, these behaviors are not considered to be signs of consciousness as regards the diagnostic criteria of the VS published by the Multi-Society Task Force on PVS [25]. In fact, it has to be acknowledged that our current understanding of residual perception in VS and MCS is incomplete and awaits future studies employing standardized and validated clinical tools for the assessment of nociception confronted to functional fMRI [8].

In conclusion, the detection of nociception in VS and MCS patients remains challenging. Developing and validating a scale, such as the Nociception Coma Scale, constitutes the first step to a better management of patients recovering from coma. Further studies are needed to further investigate the validity of our scale in a larger pool of patients and additional functional neuroimaging studies will aim to identify the subcortical and cortical correlates of NCS assessment scores".

Conflict of interest

The authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.pain.2009.09.028](https://doi.org/10.1016/j.pain.2009.09.028).

References

- [1] Boly M, Faymonville ME, Schnakers C, Peigneux P, Lambermont B, Phillips C, Lancellotti P, Luxen A, Lamy M, Moonen G, Maquet P, Laureys S. Perception of

- pain in the minimally conscious state with PET activation: an observational study. *Lancet Neurol* 2008;7:1013–20.
- [2] Boly M, Faymonville ME, Peigneux P, Lambermont B, Damas F, Luxen A, Lamy M, Moonen G, Maquet P, Laureys S. Cerebral processing of auditory and noxious stimuli in severely brain injured patients: differences between VS and MCS. *Neuropsychol Rehabil* 2005;15:283–9.
- [3] Buttner W, Finke W. Analysis of behavioural and physiological parameters for the assessment of postoperative analgesic demand in newborns, infants and young children: a comprehensive report on seven consecutive studies. *Paediatr Anaesth* 2000;10:303–18.
- [4] Chatelle C, Vanhauzenhuysse A, Mergam AN, De Val M, Majerus S, Boly M, Bruno MA, Boveroux P, Demertzi A, Gosseries O, Ledoux D, Peigneux P, Salmon E, Moonen G, Faymonville ME, Laureys S, Schnakers C. Pain assessment in non-communicative patients. *Rev Med Liege* 2008;63:429–37.
- [5] Feldt KS. The checklist of nonverbal pain indicators. *Manag Nurs* 2000;1:13–21.
- [6] Giacino J, Kalmar K, Whyte J. The JFK coma recovery scale-revised: measurement characteristics and diagnostic utility. *Arch Phys Med Rehabil* 2004;85:2020–9.
- [7] Giacino J, Ashwal S, Childs N, Cranford R, Jennett B, Katz DI, Kelly JP, Rosenberg JH, Whyte J, Zafonte RD, Zasler ND. The minimally conscious state: definition and diagnostic criteria. *Neurology* 2002;58:349–53.
- [8] Giacino J, Hirsch J, Schiff N, Laureys S. Functional neuroimaging applications for assessment and rehabilitation planning in patients with disorders of consciousness. *Arch Phys Med Rehabil* 2006;87:567–76.
- [9] Halliburton JR. Awareness during general anesthesia: new technology for an old problem. *CRNA* 1998;9:39–43.
- [10] Herr K, Coyne PJ, Key T, Manworren R, McCaffery M, Merkel S, Pelosi-Kelly J, Wild L. Pain assessment in the nonverbal patient: position statement with clinical practice recommendations. *Pain Manag Nurs* 2006;7:44–52.
- [11] Hummel P, van Dijk M. Pain assessment: current status and challenges. *Semin Fetal Neonatal Med* 2006;11:237–45.
- [12] IASP. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms. Task force on taxonomy, vol. Suppl 3. Seattle: IASP Press; 1994.
- [13] Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–74.
- [14] Laureys S, Faymonville ME, Peigneux P, Damas P, Lambermont B, Del Fiore G, Degueldre C, Aerts J, Luxen A, Franck G, Lamy M, Moonen G, Maquet P. Cortical processing of noxious somatosensory stimuli in the persistent vegetative state. *NeuroImage* 2002;17:732–41.
- [15] Laureys S, Boly M. What is it like to be vegetative or minimally conscious? *Curr Opin Neurol* 2007;20:609–13.
- [16] Lawrence J, Alcock D, McGrath P, Kay J, MacMurray SB, Dulberg C. The development of a tool to assess neonatal pain. *Neonatal Netw* 1993;12:59–66.
- [17] Loeser JD, Treede RD. The Kyoto protocol of IASP basic pain terminology. *Pain* 2008;137:473–7.
- [18] Majerus S, Gill-Thwaites H, Andrews K, Laureys S. Behavioral evaluation of consciousness in severe brain damage. *Prog Brain Res* 2005;150:397–413.
- [19] Merkel SI, Shayevitz JR, Voepel-Lewis T, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nurs* 1997;23:293–7.
- [20] Schnakers C, Zasler ND. Pain assessment and management in disorders of consciousness. *Curr Opin Neurol* 2007;20:620–6.
- [21] Schnakers C, Laureys S, Faymonville ME. Ethical implications: pain, coma, and related disorders. In: Banks W, editor. *Encyclopedia of consciousness*, vol. 1. Amsterdam: Elsevier; 2009. p. 243–50.
- [22] Stevens R, Nyquist P. Coma, delirium, and cognitive dysfunction in critical illness. *Crit Care Clin* 2006;22:787–804.
- [23] Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974;2:81–4.
- [24] The management of persistent pain in older persons. *J Am Geriatr Soc* 2002;50:S205–24.
- [25] The Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (1). *N Engl J Med* 1994;330:1499–1508.
- [26] Treede RD, Kenshalo DR, Gracely RH, Jones AK. The cortical representation of pain. *Pain* 1999;79:105–11.
- [27] Warden V, Hurley AC, Volicer L. Development and psychometric evaluation of the pain assessment in advanced dementia (PAINAD) scale. *J Am Med Dir Assoc* 2003;4:9–15.