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ORIGINAL RESEARCH

Assessment of Nociception and Pain in Participants in an Unresponsive or Minimally Conscious State After Acquired Brain Injury: The Relation Between the Coma Recovery Scale—Revised and the Nociception Coma Scale—Revised

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Abstract

Objectives: To investigate the relation between consciousness and nociceptive responsiveness (ie, Nociception Coma Scale—Revised [NCS-R]), to examine the suitability of the NCS-R for assessing nociception in participants with disorders of consciousness (DOC), and to replicate previous findings on psychometric properties of the scale.

Design: Specialized DOC program.

Setting: Specialized DOC program and university hospitals.

Participants: Participants (N = 85) diagnosed with DOC.

Interventions: Not applicable.

Main Outcome Measures: We prospectively assessed consciousness with the Coma Recovery Scale—Revised (CRS-R). Responses during baseline, non-noxious, and noxious stimulations were scored with the NCS-R and CRS-R oromotor and motor subscales.

Results: CRS-R total scores correlated with NCS-R total scores and subscores. CRS-R motor subscores correlated with NCS-R total scores and motor subscores, and CRS-R oromotor subscores correlated with NCS-R total scores as well as verbal and facial expression subscores. There was a difference between unresponsive wakefulness syndrome and minimally conscious state in the proportion of grimacing and/or crying participants during noxious conditions. We replicated previous findings on psychometric properties of the scale but found a different score as the best threshold for nociception.

Conclusions: We report a strong relation between the responsiveness to nociception and the level of consciousness. The NCS-R seems to be a valuable tool for assessing nociception in an efficient manner, but additional studies are needed to allow recommendations for clinical assessment of subjective pain experience.

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A minority of persons with severe brain injuries remain in a state of severely disordered consciousness (DOC) beyond the acute phase. In the vegetative state (also called unresponsive wakefulness syndrome [UWS][1]), patients will show only reflexive movements, whereas in a minimally conscious state (MCS), patients demonstrate reproducible but fluctuating voluntary behaviors without functional communication.[2] Both UWS and MCS may last for weeks or months or become chronic,[3,4] although with a higher proportion of functional recovery of MCS vs UWS.[4,5]

Care for patients with DOC who are, by definition, unable to communicate their own experiences is a huge challenge for caregivers and families.[6] A frequent question raised by caregivers and relatives of patients with DOC is whether their loved ones are suffering from either physical or psychological pain.[7,8] As far as physical pain is concerned, severely brain injured persons show many comorbidities and medical complications that may trigger pain, both in the acute and the post-acute phase.[9] Potential causes of pain in the chronic phase are spasticity,[10] contractures, pressure ulcers, soft tissue ischemia, peripheral nerve injuries, and premorbid painful conditions.[11] Patients might also suffer from painful conditions related to disturbances in the network involved in pain perception[12,13] or, in general, malfunctions of the sensory processing of physical stimuli (eg, allodynia, central post stroke pain[14]).

Several neuroimaging studies investigating nociceptive (ie, *neural process of encoding noxious stimuli*) and pain (ie, *unpleasant sensory and emotional experience associated with real or potential tissue damage*[15]) processing in participants in an UWS and MCS suggest that UWS is associated with a severe cortico-subcortical disconnection in response to noxious stimulation[12,13] whereas participants in a MCS show preserved cortical responses similar to participants without brain injury,[12] suggesting a higher probability of subjectively experiencing pain in MCS.

However, other studies[16-18] reported complex cortical responses to nociceptive and emotional stimuli in UWS, suggesting that a subgroup of participants behaviorally unresponsive could retain cortical abilities for pain and emotional perception.

Because pain treatment is generally tailored to the subjective experience of a patient, pain management in patients with DOC constitutes a clinical and ethical challenge, and alternative methods based on behavioral responses at bedside are necessary.[7] Numerous behavioral scales for pain assessment have been developed and well-validated for noncommunicative patients, such as patients with dementia and newborns,[19-22] but until recently, there have been few scales developed specifically to assess pain in noncommunicative patients with severe brain injury. For example, the Behavioral Pain Scale[23] and the Critical Care Pain Observation Tool[24] have been developed for noncommunicative and sedated adult patients in intensive care.

Recently, new scales have also been proposed such as the Scale of Behavior Indicators of Pain (Escala de Conductas Indicadoras de Dolor[25]) for ventilated critically ill patients and the "Zurich Observation Pain Assessment" for patients with major cognitive impairments or DOC[26]; however, these scales have not been widely used, partly because of limited validation data.

List of abbreviations:

CRS-R Coma Recovery Scale—Revised
DOC disorders of consciousness
MCS minimally conscious state
NCS-R Nociception Coma Scale—Revised
UWS unresponsive wakefulness syndrome

In 2012, a standardized behavioral nociception scale adapted for patients with chronic and acute DOC was introduced—the Nociception Coma Scale—Revised (NCS-R).[27,28] It was based on behaviors included in previously validated scales for noncommunicative patients as well as the diagnostic criteria and responses described specifically in DOC.[2,29] The NCS-R has been shown to have good interrater reliability and concurrent validity with other scales developed for noncommunicative patients (eg, patients with dementia, newborns).[27,28] In line with previous neuroimaging studies[27,28] investigating brain activity related to nociceptive stimulation in participants with DOC, total scores differ according to the level of consciousness, with participants in a MCS showing higher scores than do those in an UWS. However, the exact relation between NCS-R scores and the level of consciousness remains unclear. There is thus a need for more studies exploring the relation between the level of consciousness, nociception, and the behavioral expression of pain experience.

The present study aimed to investigate (1) the relation between behavioral signs of consciousness as assessed by the Coma Recovery Scale—Revised (CRS-R[29]) and responsiveness to nociception (ie, NCS-R[27]) and (2) the sensitivity of the NCS-R compared to the CRS-R for assessing nociception in noncommunicative participants with severe brain injury. In addition, we wanted to replicate previous findings (ie, sensitivity and cutoff score for nociception).

We hypothesized that (1) the level of consciousness will be positively correlated with NCS-R scores and (2) the NCS-R will be more sensitive to characterize nociceptive processing than the CRS-R. We also expected to replicate previous data on the NCS-R sensitivity to nociception and the cutoff score of 4 previously defined as the threshold for suggesting the presence of potential pain .[27]

Methods

Population

Participants were prospectively enrolled in 6 centers across Europe and in the United States between May 9, 2013 and May 31, 2016.

Inclusion criteria were (1) age ≥16 years at the time of the assessment; (2) documented acquired brain injury; (3) no sedation/centrally acting drugs (benzodiazepine, long-acting sedating drugs) administered within 48 hours before the assessment; and (4) clinical state of UWS[1,30] or MCS,[2] as documented with the CRS-R, at the time of inclusion.

Exclusion criteria were (1) documented history of brain injury before the one causing DOC and (2) premorbid history of developmental, psychiatric, or neurological illness resulting in documented functional disability up to the time of the injury.

Before inclusion in the study, informed consent was obtained by the participants' legal guardians. The study was approved by the local ethics committees at each site.

Study design

All participants were assessed by 1 examiner who had undergone a formal training in CRS-R and NCS-R assessments and who had several years of experience in the assessment of

consciousness with the CRS-R. Both scales were applied in a single session (see table 1 for a comparative description of both scales). Participants were assessed in a sitting position. Each session started with a 1-minute baseline observation and scoring of the spontaneous behaviors at rest according to the CRS-R and NCS-R guidelines.

The CRS-R consists of 23 hierarchically arranged items that comprise 6 subscales addressing 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.[29] It has strong evidence of reliability and validity for the assessment of patients with DOC on the basis of a systematic review completed by the Clinical Practice Committee of the American Congress of Rehabilitation Medicine.[31] The diagnostic criteria for coma, UWS, MCS, and emergence from MCS are embedded within the scale. The NCS-R includes 3 subscales assessing motor, verbal, and facial expression responses to nociception, with a total score ranging from 0 to 9. Its psychometric properties have been reported in previous studies, as presented in the introduction section.

1. The CRS-R was administered using its standard protocol.[29] When applying bilateral noxious stimulation (motor item 3-assessing localisation to pain, ie, *squeeze the finger or toe between your thumb and index finger*, 2 trials on each side for 5 seconds; and motor item 2 - assessing reflexive response to pain, ie, *press the ridge of a pencil into the cuticle of each 4 extremities*), the highest responses on each side were scored on both the CRS-R and the NCS-R. If the patient achieved a motor subscale score of $\geq$4 on the CRS-R, noxious stimulation was applied anyway (starting with the motor item 3 and then applying stimulation of motor item 2 if absence of response). Responses to noxious stimuli were scored with the NCS-R as well as the motor and oromotor subscales of the CRS-R. The CRS-R assessment was then resumed.
2. In addition, non-noxious stimulation was administered (5 taps on each hand according to Gill-Thwaites et al[32]) and responses were scored with the NCS-R as well as the motor and oromotor subscales of the CRS-R. The initial side of stimulation (left/right vs right/left) and order of stimulation type (starting with A or B) were pseudo-randomized using a Matlab script (R2013b)[a] to have the same number of participants in each condition.

Table 1 Description of items included in the CRS-R and NCS-R

	Item	
Subscale	CRS-R	NCS-R
Auditory	4: Consistent movement to command	NA
	3: Reproducible movement to command	
	2: Localization to sound	
	1: Auditory startle	
	0: None	
Visual	5: Object recognition	NA
	4: Object localization: reaching	
	3: Visual pursuit	
	2: Fixation	
	1: Visual startle	
	0: None	
Motor	6: Functional object use	3: Localization to noxious stimulation
	5: Automatic motor response	2: Flexion withdrawal
	4: Object manipulation	1: Abnormal posturing
	3: Localization to noxious stimulation	0: None/flaccid
	2: Flexion withdrawal	
	1: Abnormal posturing	
	0: None/flaccid	
Oromotor/verbal	3: Intelligible verbalization	3: Verbalization (intelligible)
	2: Vocalization/oral movement	2: Vocalization
	1: Oral reflexive movement	1: Groaning
	0: None	0: None
Facial expression	NA	3: Cry
		2: Grimace
		1: Oral reflexive movement/startle response
		0: None
Communication	2: Functional: accurate	NA
	1: Nonfunctional: intentional	
	0: None	
Arousal	3: Attention	NA
	2: Eye opening without stimulation	
	1: Eye opening with stimulation	
	0: Unarousable	

Abbreviation: NA, not applicable

Statistical analysis

The number of participants expected to be included during the study period was between 80 and 100. Restricting the analysis to correlation analysis between the NCS-R and the CRS-R, we found that a sample size of 85 would be sufficient to detect a correlation coefficient of 0.3 (medium effect size) with a power of 80%.

Independent *t* tests and chi-square analyses were performed to assess the demographic and clinical differences between MCS and UWS. Spearman correlations were computed to assess the relation between CRS-R total scores and NCS-R total scores and subscores as well as between CRS-R motor and oromotor subscores and NCS-R total scores and subscores (using false discovery rate correction for multiple comparisons[33]).

To examine the ability of the NCS-R vs the CRS-R to assess nociceptive responsiveness, the frequency of participants displaying responses to noxious stimuli assessed by the NCS-R items in UWS vs MCS was explored (specifically for grimacing and crying—items that are not part of the CRS-R). A Fisher exact test (1-sided) was conducted to assess the difference between MCS and UWS in the proportion of grimacing and/or crying participants during non-noxious and noxious conditions.

Finally, a Friedman analysis of variance was performed using NCS-R total scores during baseline, non-noxious, and noxious conditions to assess the sensitivity of the NCS-R to nociceptive responsiveness. In addition, Mann-Whitney analyses were used to compare NCS-R scores between participants in an UWS and those in a MCS. A Wilcoxon signed-rank test was then conducted for post hoc analyses. A receiver operating characteristic analysis was also performed on NCS-R total scores (non-noxious vs noxious) to define the best threshold that would differentiate non-noxious from noxious stimulation for the whole group and for participants in an UWS and MCS, as well as in different etiologies (ie, traumatic, anoxic, other).

The results were considered significant at $P<.05$.

Results

Eighty-five participants were included in the study; 57 of them were diagnosed with MCS and 28 with UWS according to CRS-R diagnostic criteria (for details, see table 2). Thirty-five participants had a traumatic etiology, 26 anoxic brain injuries, and 24 other nontraumatic etiologies (eg, stroke, encephalopathy). There was no difference in sex, mean age, time since insult, and presence of tracheostomy between participants in an UWS and those in a MCS. CRS-R scores and etiology differed between the groups. Table 3 reports all the correlation data for the following analyses.

For the whole group, correlations were found between CRS-R total scores and NCS-R total scores (fig 1) and subscores in response to noxious stimulation. When focusing on the level of consciousness, CRS-R total scores also correlated with NCS-R total scores and motor subscores in participants in a MCS and only with motor subscores in those in an UWS.

CRS-R motor subscores correlated with NCS-R total scores and motor subscores for the whole group as well as in MCS and only with motor subscores in UWS. CRS-R oromotor subscores correlated with NCS-R total scores and verbal and facial expression subscores for the whole group, with NCS-R total scores and verbal subscores in MCS and NCS-R total scores and facial expression subscores in UWS.

Descriptive statistics for NCS-R facial expression subitems report the importance of the facial expression subscale for grimace and cry in response to nociception (all: grimace: 38%, cry: 8%; UWS: grimace: 18%, cry: 4%; MCS: grimace: 47%; cry: 11%) (fig 2). This was confirmed by the Fisher exact test, reporting a difference between UWS and MCS in the proportion of grimacing and/or crying participants only during the noxious condition ($P=.001$) but not during the non-noxious condition ($P=0.5$) (all: grimace: 6%, cry: 0%; UWS: grimace: 4%, cry: 0%; MCS: grimace: 7%; cry: 0%). Because verbal and also partially facial expression (eg, crying) depend on the ability to produce sounds that is affected by the presence and type of tracheostomy, further comparisons were done between the group that could produce sound (ie, absence of tracheostomy, fenestrated/speaking valve or closed tracheostomy) and the group that could not (ie, nonfenestrated cuffed tracheostomy). The proportion of participants with the ability to produce sound vs those without differed according to the diagnosis (ie, UWS vs MCS; $\chi^2=4.3$; $P=.04$). A Mann-Whitney analysis (U) was used to assess the difference in NCS-R facial expression and verbal subscores between those groups. The results showed a difference in both facial expression

Table 2 Demographic and clinical data

Characteristic	MCS (n=57)	UWS (n=28)	*P* Value for Statistical Difference
Female/male sex	20/37 (35/65)	8/20 (29/71)	0.6
Age (y)	42.5±17.3	48±17.4	0.3
Days postonset	133 (IQR, 77.5—350; range, 12—9911)	142 (IQR, 87.5—396; range, 13—3696)	0.07
Etiology			<.05
TBI	25 (44)	10 (36)	
Anoxic	12 (21)	13 (46)	
Other (non—traumatic)	20 (35)	5 (18)	
Tracheal tube			
None	31 (54)	7 (25)	.056
Cuffed nonfenestrated	23 (40)	18 (64)	
Cuffed/speaking valve	1 (2)	2 (7)	
Cap	2 (4)	1 (4)	
CRS-R score	9.8±4.0	4.7±1.4	<.001

NOTE. Values are mean ± SD, median (IQR), or n (%).
Abbreviations: IQR, interquartile range; NS, nonsignificant; TBI, traumatic brain injury.

Table 3 Spearman correlations (and *P* values) between NCS-R total scores and subscores in response to nociception, CSR-R total scores, and CRS-R M and CRS-R O subscores in response to nociception

	All				UWS				MCS			
Measure	NCS-R Total	NCS-R M	NCS-R V	NCS-R FE	NCS-R Total	NCS-R M	NCS-R V	NCS-R FE	NCS-R Total	NCS-R M	NCS-R V	NCS-R FE
CRS-R total	**.41 (.002)****	**.66 (<.0001)*****	**.26 (.02)***	**.34 (.001)****	.26 (.02)	**.62 (<.0001)*****	.42 (.03)*	.19 (.33)	**.41 (.002)****	**.61 (<.0001)*****	.07 (.59)	.15 (.27)
CRS-R M	**.46 (<.0001)*****	**.98 (<.0001)*****	.10 (.38)	.05 (.64)	.38 (.05)*	**.93 (<.0001)*****	.27 (.16)	.03 (.9)	**.38 (.003)****	**.99 (<.0001)*****	−.04 (.79)	−.06 (.64)
CRS-R O	**.55 (<.0001)*****	.06 (.57)	**.67 (<.0001)*****	**.43 (<.0001)*****	**.50 (.007)****	.23 (.23)	.37 (.06)	**.59 (.001)****	**.53 (<.0001)*****	−.12 (.44)	**.71 (<.0001)*****	.29 (.03)*

NOTE. *$P<.05$; **$P<.01$; ***$P<.001$. Bold numbers highlight correlations that remained significant after correction for multiple comparisons.
Abbreviations: CRS-R M, Coma Recovery Scale—Revised motor; CRS-R O, Coma Recovery Scale—Revised oromotor; NCS-R FE, Nociception Coma Scale—Revised facial expression; NCS-R M, Nociception Coma Scale—Revised motor; NCS-R V, Nociception Coma Scale—Revised verbal.

($U=1215.5$; $P=.01$) and verbal ($U=1117.5$; $P=.01$) subscores, suggesting an effect of tracheostomy on these scores.

Finally, the Friedman analysis of variance highlighted a difference in NCS-R total scores between baseline, non-noxious, and noxious conditions ($\chi^2=336.9$; $P<.001$). Post hoc analyses showed a difference between noxious and baseline conditions (Wilcoxon test $[W]=3388$; $P<.001$) and between noxious and non-noxious conditions ($W=30.5$; $P<.001$), but not between baseline and non-noxious conditions. A difference in NCS-R total scores was observed according to the diagnosis, with lower scores observed in participants in an UWS ($U=1176.5$; $P<.001$).

A score of ≥ 2 was defined as the best threshold for nociception with a sensitivity of 91% and a specificity of 88% for the whole group. The same threshold was obtained for each level of consciousness separately (UWS: sensitivity, 79%; specificity, 82%; MCS: sensitivity, 97%; specificity, 91%), and it did not differ according to the etiology (traumatic: sensitivity, 91.4%; specificity, 94.3%; anoxic: sensitivity, 84%; specificity, 84%; other: sensitivity, 96%; specificity, 84).

Discussion

The aim of the present study was to investigate the relation between behavioral signs of consciousness as assessed by the CRS-R and responsiveness to nociception as assessed by the NCS-R. The results support the hypothesis of a strong relation between the responsiveness to nociception and the level of consciousness, where higher levels of consciousness (ie, CRS-R total scores) were associated with higher behavioral responsiveness (ie, NCS-R total scores) to noxious stimulation. This was also reflected in higher total scores on the NCS-R in participants in a MCS compared with those in UWS. A further objective was to examine the suitability of the NCS-R for assessing nociception as compared with the CRS-R. The CRS-R motor and oromotor subscores after noxious stimulation correlated strongly with the NCS-R total scores during noxious stimulation. Hence, the results did not support our hypothesis that the NCS-R is significantly more sensitive than the CRS-R in assessing nociception in noncommunicative participants with severe brain injury. If the high correlation between the CRS-R oromotor and motor subscores and nociceptive scores can likely be explained by high item overlap between the motor and verbal/oromotor subscales of the 2 scales,[27,29] there is a certain circularity because of the overlap between the level of consciousness and pain perception that cannot be solved by designing new assessment tools, because patients in an UWS probably do not react to nociception in the same way as do patients in a MCS. Although we cannot resolve this question here, in terms of available assessment tools, the CRS-R is a comprehensive tool for assessing consciousness with 6 subscales whereas the NCS-R is specifically designed to assess reactivity to noxious stimuli by focusing on verbal, motor, and facial responsiveness in a condensed/time-efficient manner. The observation of facial expression may add information in the context of diagnoses of pain perception. We highlighted the interest of that subscale in our descriptive statistics, showing that grimacing was observed more frequently in response to nociception (grimace and cry: 38% and 8% of the participants vs 6% and 0% in the non-noxious condition, respectively) and that there was a difference between MCS and UWS in the proportion of grimacing and crying participants during noxious stimulation but not during non-noxious stimulation. This could partly be

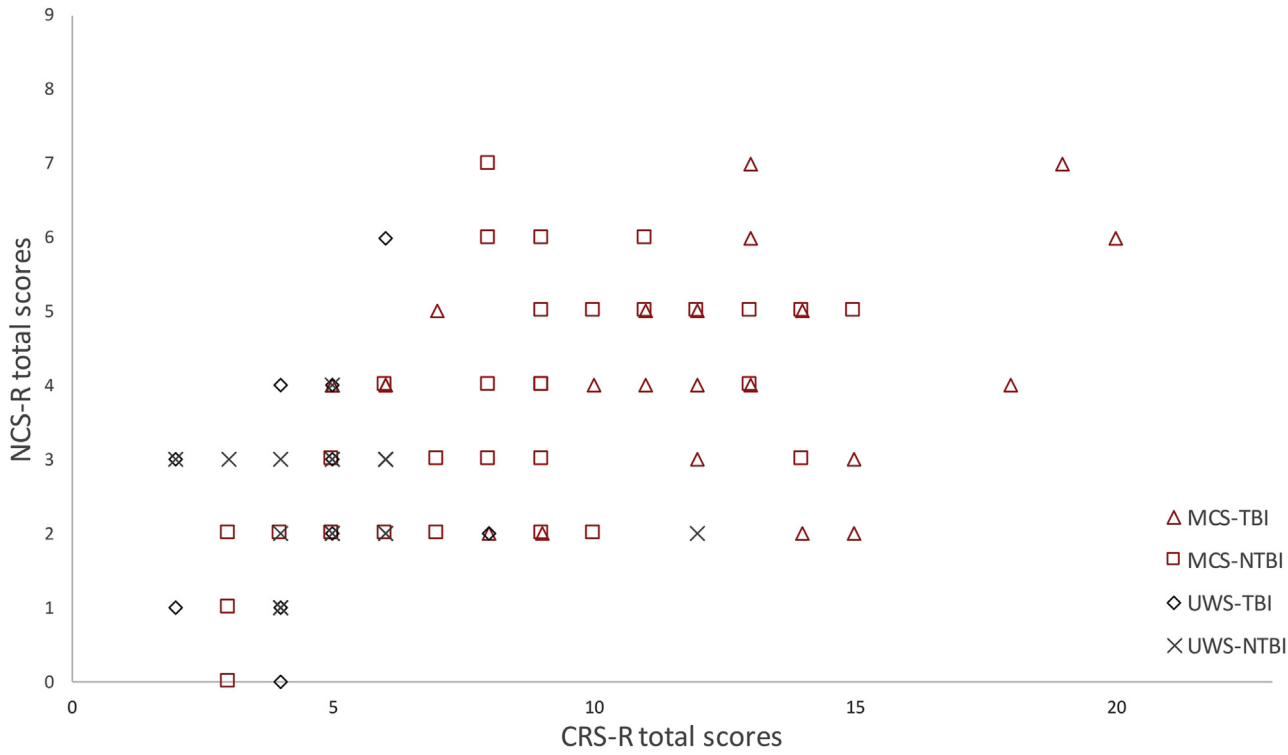

Fig 1 Scatterplot of the NCS-R total scores and CRS-R total scores during noxious stimulation. Abbreviations: NTBI, non—traumatic brain injury; TBI, traumatic brain injury.

explained by the fact that the presence of nonspeaking tracheostomy (more commonly observed in participants in an UWS than in those in a MCS) was associated with lower facial responsiveness (ie, lower facial expression subscores). This observation is important because it highlights the importance of carefully interpreting NCS-R scores depending on the patient's condition.

An additional aim was to replicate previous findings on the NCS-R sensitivity and cutoff score for pain. We observed higher NCS-R scores during the noxious condition than during both baseline and non-noxious conditions, thus replicating previous findings that have shown NCS-R to be sensitive for assessing responses to noxious stimulation and that it is possible to disentangle responses to noxious and somatosensory stimuli.[27] However, the threshold of 4 previously reported[27] as the best cutoff scores was not confirmed in this study. Instead, a score of 2 was suggested to be more appropriate to detect potential nociception in DOC (and in both UWS and MCS separately). However, a cutoff score in the sense of a clear indication for need of treatment of nociception in general is of limited clinical utility for inferring subjective pain experience in persons with DOC, because it is possible to detect nociceptive responses at a reflexive level that does not automatically imply conscious pain perception. Detecting nociceptive responses in patients with DOC does not necessarily infer subjective pain perception, because this is strongly related to the person's cognitive processing capacity. If the detection of nociception in conscious/unconscious patients is of interest to detect potential medical complications or prevent the development of chronic pain, for example, we are still far from establishing precise recommendations for clinical thresholds for subjective pain experience. This correspondingly leads to a

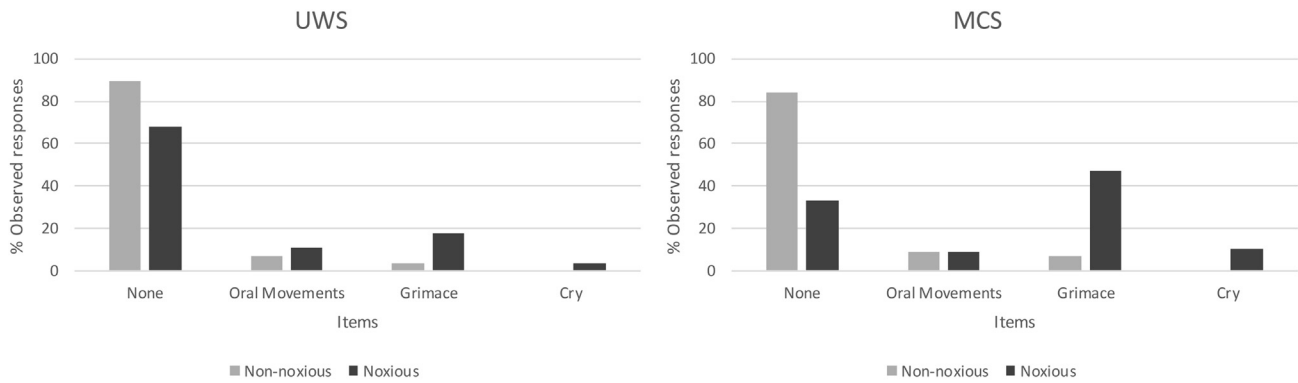

Fig 2 Percentages of responses to non-noxious and noxious stimulation observed on the facial expression subscale in participants in an UWS and MCS.

concern that a preserved capacity for subjective pain perception can go undetected in patients with DOC. Because several studies[12,13,16,17,34] suggested the possibility for patients behaviorally diagnosed with UWS of retaining the capacity for subjective pain perception, we still do not know much about the functioning of pain networks in general and in individual patients. Do they process pain caused by nociception in their sensory, cognitive, or affective system so that they experience suffering and are conscious of that? Do they retain affective consciousness in the sense that they suffer when confronted with the suffering of others? Do they experience pain without obvious nociception?

With regard to pain management and medication, there is a complex decision to be made in that potentially sedating effects of pain treatments may hide the individual responsiveness (ie, sedation) but persistent pain might be a stressor negatively influencing recovery. It is therefore of great importance to carefully monitor patients when assessing and treating potential pain. Given the present results, we would suggest avoiding the use of a specific threshold for determining whether a patient needs pain treatment. Instead, in addition to carefully observing and monitoring the patient's behavior, we recommend a regular monitoring of the patient using the NCS-R, looking for (1) changes in scores (ie, increase, suggestive of medical complication/potentially painful condition); (2) increase in scores during potentially painful conditions (eg, care, mobilization); and (3) scores during potentially painful conditions equal to or higher than what are observed during noxious stimulation (ie, nail-bed pressure).

Study limitations

A major limitation of the study is the high overlap of the items in the 2 assessment scales used here. We decided to use the CRS-R because it is the most commonly used and validated scale for assessing consciousness in patients with DOC, but we could have added additional behavioral scales. The question remains whether the NCS-R is sufficient for the assessment of patients with DOC. For example, it does not contain items related to vegetative responses to nociceptive stimuli (eg, changes in respiration, heart rate, sweating). However, the high interdependency between the level of consciousness and pain perception is most probably not just reflecting psychometric issues in the scales, because existing studies give reason to believe that there are phenomenological differences in pain processing and experience depending on the level of consciousness. Another limitation concerns lack of blinding, because the same raters conducted both measures; thus, raters were not masked to the results of one measure vs the other. Finally, the diagnoses used for group analyses were based on a single CRS-R assessment. Given the known fluctuations in responsiveness to the relatively high diagnostic error rate,[35] multiple administrations of the CRS-R would be preferable to ensure a reliable diagnosis.

Conclusions

The main aim of the present study was to investigate the relation between behavioral signs of consciousness as assessed by the CRS-R and responsiveness to nociception as assessed by the NCS-R. We here report a strong relation between the responsiveness to nociception and the level of consciousness. If our results did not support the hypothesis that the NCS-R is significantly more sensitive than the CRS-R in assessing nociception in noncommunicative participants with severe brain-injury, we replicated previous data on the NCS-R sensitivity to nociception. However, we did not confirm the previously defined threshold, highlighting the need for further research. Future studies should assess the effect of analgesic treatments on pain perception and responsiveness (ie, NCS-R) and level of consciousness in this population to better understand the relation between the NCS-R and the CRS-R. Additional studies on the NCS-R should also aim at better defining the best threshold to be used to assess nociception and/or pain by using a different kind of stimulation with various levels of intensity (eg, to account for saliency[36,37]).

Supplier

a. Matlab script; The MathWorks, Inc.

Keywords

Brain injuries; Consciousness disorders; Nociception; Outcome assessment; Pain; Rehabilitation

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