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Research paper

Discriminative ability of the Behavioural Indicators of Pain Scale-Brain Injury (Escala de Conductas Indicadoras de Dolor-Daño Cerebral) according to level of sedation in critically ill patients with acquired brain injury and disorders of consciousness: A multicentre observational study

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ABSTRACT

Background: Appropriate assessment of pain is essential to ensure effective treatment.
Objectives: The objective of this study was to determine the discriminative ability of the Behavioural Indicators of Pain Scale-Brain Injury (Escala de Conductas Indicadoras de Dolor-Daño Cerebral [ESCID-DC]) under different sedation levels (deep vs. light-to-moderate) and procedures in critically ill patients with acquired brain injury and disorders of consciousness.
Methods: A multicentre, observational study was conducted involving critically ill patients with acquired brain injury and an artificial airway unable to self-report. Patients with prior brain injuries, cognitive impairment, or any condition (clinical or pharmacological) affecting motor response were excluded. The ESCID-DC was administered 5 min before, during, and 15 min after performing painful procedures (tracheal suctioning, right/left nail bed pressure) and a nonpainful procedure (gauze pad rubbing). All assessments were repeated under deep and light-to-moderate sedation.
Results: A total of 418 patients (284 men; 68%) were enrolled. The mean (standard deviation) age was 56.2 (16.3) years. Pain was assessed in 369 patients under deep sedation and in 346 under light-to-moderate sedation. Median (interquartile range) Glasgow Coma Scale scores were 6 (4–7) and 8.5 (7–9) in the deep and light-to-moderate sedation groups, respectively. Under deep sedation, median pain scores during the suctioning and pressure procedures were, respectively, 3 (2–5) and 0 (0–2). Median ESCID-DC scores under light-to-moderate sedation during suctioning and right and left nail bed pressure were 6 (4–7), 3 (1–4), and 3 (1–5), respectively. The ESCID-DC score during the nonpainful procedure was 0. During tracheal suctioning, the discriminative ability of the ESCID-DC was adequate (area under the curve = 0.88; 95% confidence interval: 0.84–0.93), even in patients with very low levels of

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consciousness. For the pressure procedures, discriminative ability was adequate only when the Glasgow Coma Scale score was ≥5.
Conclusions: The discriminative ability of the ESCID-DC depends on the level of consciousness and type of procedure. In patients with a low level of consciousness, the scale has a limited capacity to detect pain during less painful procedures.

1. Introduction

Pain is defined as "*An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage*".[1] Pain is common in critically ill patients who are unable to self-report, regardless of the specific underlying primary condition. Care-related procedures are one of the main causes of pain in this patient population, with reported prevalence rates of up to 90%.[2,3] In patients whose ability to communicate is impaired or absent, pain often remains undetected and undertreated. This is highly relevant because inadequate pain management in the intensive care unit (ICU) can lead to agitation and delirium, increase the need for mechanical ventilation, and may even prolong the hospital stay.[4–6] Moreover, in brain-injured patients, exposure to pain can exacerbate the condition.[7,8] In the long term, uncontrolled pain is associated with an increased risk of post-traumatic stress disorder and the development of chronic pain.[9–12]

An accurate assessment of pain is essential to ensure effective treatment. Several behaviour-based pain assessment tools have been adapted and validated for use in specific populations such as critically ill patients with acquired brain injury and disorders of consciousness.[13–16] Several specific behavioural responses to pain have been documented in this patient population, although the intensity of the response depends on the level of consciousness.[17–20] The behavioural response measured by pain assessment tools is also dependent on the level of sedation, although the influence of sedation levels (i.e., deep vs. light-to-moderate sedation) on the discriminative ability of these instruments is not well understood.[13]

The Behavioural Indicators of Pain Scale (*Escala de Conductas Indicadoras de Dolor* [ESCID]) is a behavioural pain assessment tool that has been validated in medical and surgical patients.[21] In patients with acquired brain injury and disorders of consciousness, this tool has shown the ability to discriminate between painful and nonpainful procedures; however, it has certain item-level limitations. Consequently, the ESCID is not entirely adequate to detect pain-related behavioural responses in this specific patient population. Furthermore, although the available data suggest that the ESCID score depends in part on the level of consciousness and/or degree of sedation, this critical aspect has not been explored in depth.[18,20]

Given the limitations of the original ESCID, this scale was recently adapted and validated for patients with acquired brain injury, disorders of consciousness, and an artificial airway. The new scale, the Behavioural Indicators of Pain Scale-Brain Injury (*Escala de Conductas Indicadoras de Dolor-Daño Cerebral* [ESCID-DC]),[22] contains eight items (behavioural indicators). Although many of the items from the original scale are included in the ESCID-DC, including "frowning", "clenched jaw", "head tilt", "eyes tightly shut", and "upper and lower limb flexion", there are several important differences between the two scales. For example, the ventilation-related behavioural indicators were refined to place a greater focus on the respiratory pattern and thoracoabdominal synchrony. In addition, the "consolability" item was renamed as "inconsolability". Another important difference is that the ESCID-DC items evaluate only a single behavioural response, whereas the items on the original scale evaluated several different responses. A psychometric evaluation of the ESCID-DC confirmed the validity and reliability of this tool, which shows good internal consistency (Cronbach's alpha ≥0.80), good discriminant validity for painful procedures (area under the curve [AUC] > 0.7), and strong interobserver agreement.[22]

Both the ESCID and the ESCID-DC were designed to be administered under light or moderate sedation to reliably detect behavioural responses in patients with acquired brain injury and disorders of consciousness.[16,23] Given that many ICU patients require deep sedation in the first several days following ICU admission, these tools cannot be administered until a median of 7 days from admission[22] or even longer (median: 13 days) in some cases.[24] As a result, there is a significant time gap between ICU admission and the initial pain assessment during which pain cannot be adequately monitored.

The ESCID-DC is a new scale, and its capacity to reliably identify painful behaviours at different levels of sedation has not been assessed.[22] As a result, the discriminative ability of the ESCID-DC in patients under deep sedation is not known, nor do we know if the ESCID-DC could be applied earlier in the ICU stay to accurately determine the presence of pain. These questions need to be resolved before we can establish criteria to facilitate the interpretation of behavioural responses in patients under deep sedation, which would then allow us to define more effective pain management strategies.

In this context, the primary objective of the present study was to determine the discriminative ability of the ESCID-DC in critically ill patients with acquired brain injury and disorders of consciousness according to the sedation level (deep vs. light-to-moderate) and type of procedure. A secondary objective was to evaluate differences in ESCID-DC scores across different conditions (type of procedure, level of consciousness, degree of sedation, and brain injury aetiology).

2. Methods

2.1. Design and setting

This prospective, longitudinal, multicentre observational study was carried out at 21 ICUs (17 hospitals) within the Spanish National Health System.

2.2. Study population and sample size

The sample size was based on the primary endpoint (ESCID-DC pain score). To construct a 95% confidence interval (CI) for an estimated AUC of 0.7 with a precision of ±0.03, a sample size of at least 332 patients was necessary.

Inclusion criteria were as follows: age ≥16 years, diagnosis of acquired brain injury (any aetiology), inability to self-report (verbal or motor), artificial airway, and signed informed consent. Exclusion criteria were as follows: previous brain injury or cognitive impairment, spinal cord injury, severe polyneuropathy, diagnosis of brain death, continuous infusion of muscle relaxants,

barbiturate coma, deep sedation level (Richmond Agitation-Sedation Scale [RASS] score = −5), and/or Glasgow Coma Scale (GCS) score = 3.

2.3. Data collection

To minimise intercentre variability, standardised criteria were established for the data collection process and administration of the ESCID-DC. Similarly, standardised training and supervision protocols were established for all participating centres. All researchers were trained in the administration of the ESCID-DC. At each centre, all researchers participated in a hands-on training session involving the administration of the scale in at least five patients under the supervision of the trainers. The ESCID-DC was evaluated independently by two blinded observers. The trainers provided feedback on each patient evaluation, with a special emphasis on scoring discrepancies between evaluators to reinforce the instructions in the ESCID-DC user guide. Inter-rater agreement showed kappa values >0.80 for all ESCID-DC items.

Pain response was assessed at three time points: 5 min before, during, and 15 min after the performance of common clinical procedures, both painful and nonpainful.[25–28] There was a 15-min washout period between each procedure.

The painful procedures consisted of tracheal suctioning and the application of pressure to the nail bed of the right and left ring fingers (or the middle finger in some cases). The AlgiScan plus® (Hagen, Germany) algometer was used to apply pressure (5–8 kg) to the nail bed until a behavioural response was obtained or for a maximum of 30 s. This pressure range was selected based on a previous pilot study conducted in a similar population.

The nonpainful procedure (used as a control) consisted of rubbing a gauze pad against an area of healthy skin on the patient's forearm (or calf, if necessary).

When feasible, pain measurements were assessed under two different levels of sedation: deep sedation (RASS score: -4) and light-to-moderate sedation (RASS score: -3 or −2). A total of 12 repeat measurements were performed per patient at each level of sedation (24 measurements in total).

To perform pain assessments under both measurement conditions (i.e., RASS score: -4 and/or RASS score: -3/-2), patients were required to have a GCS score >3 and to undergo daily monitoring to assess their levels of sedation and consciousness.

2.4. Study variables and outcome measures

The primary outcome was the pain score measured with the ESCID-DC. This scale includes eight items grouped into four categories (facial response, ventilation/breathing, bodily response, and inconsolability). Scores on each item range from 0 to 2, with total scores ranging from 0 to 16 (Table 1).[21]

Table 1
Behavioral Indicators of Pain Scale-Brain Injury (Escala de Conductas Indicadoras de Dolor-Daño Cerebral [ESCID-DC]).

Item	Categories		
	0	1	2
Tilts head: *Moves head to one or both sides*	**Neutral/no resistance:** Head in neutral position. No resistance.	**Intermittent/mild-to-moderate resistance:** Intermittent movement of head to one or both sides with or without mild-to-moderate resistance.	**Continuous/strong resistance:** Continuous movement of head to one or both sides with or without strong resistance.
Frowns/wrinkles forehead/ knits eyebrows: *Contraction of brow, forehead, or eyebrows*	**Relaxed:** Forehead, brow, and eyebrows relaxed.	**Intermittent:** Intermittently frowns, wrinkles forehead, or knits eyebrows.	**Continuous:** Continuously frowns, wrinkles forehead, or knits eyebrows.
Eye tightening: *Increased tension in the muscles of the eye orbit or eyelids.*	**Relaxed:** Eyes and eyelids relaxed.	**Intermittent:** Intermittently tightening of eyes or eyelids.	**Continuous:** Continuous tightening of eyes or eyelids.
Clenching of teeth/mouth/ jaw: *Increased tension in the mouth or jaw muscles. Teeth clenched*	**Relaxed:** Teeth, mouth, and jaw relaxed.	**Intermittent/mild-to-moderate resistance** Clenches teeth, mouth, or jaw intermittently and/or with mild-moderate resistance.	**Continuous/strong resistance:** Clenches teeth, mouth or jaw continuously and/or with strong resistance.
Ventilator asynchrony: Alarms indicate ventilatory asynchrony or lack of coordinated movement between the thorax and abdomen during ventilation	**Ventilatory synchrony without alarms:** Synchronous thoracoabdominal respiratory/ventilatory pattern. No ventilator alarms.	**Intermittent asynchrony/self-limiting alarms:** Intermittent asynchronous thoracoabdominal respiratory/ventilatory pattern. Self-limiting ventilator alarms.	**Continuous asynchrony/alarms sound continuously:** Continuous asynchronous thoracoabdominal respiratory/ventilatory pattern. Ventilator alarm sounds continuously.
Upper limb flexion: *Act of bending one or both upper limbs at the elbow, wrist, or fingers (rule out decortication/ decerebration movements).*	**Relaxed:** Upper limbs relaxed.	**Intermittent/mild-to-moderate resistance:** Intermittent flexion of one or both upper limbs (localised or withdrawal) and/or with mild-moderate resistance.	**Continuous/strong resistance:** Continuous flexion (with or without strong resistance) of one or both upper limbs (localised or withdrawal).
Lower limb flexion: *Act of bending one or both lower limbs at the knee, ankle, or bending of the toes.*	**Relaxed:** Lower limbs relaxed.	**Intermittent/mild-moderate resistance** Intermittent flexion (with or without mild-to-moderate resistance) of one or both lower limbs.	**Continuous/strong resistance:** Continuous flexion (with or without strong resistance) of one or both lower limbs.
Inconsolability: Restless. Not reassured by touch or talk.	**Relaxed:** Calm and relaxed.	**Mild-to-moderate restlessness:** Patient shows mild-moderate restlessness, but is reassured by touch or talk. Behavioural responses cease upon completion of the procedure.	**Intense restlessness:** Patient shows strong restlessness and is not reassured by touch or talk. Behavioural responses continue even after completion of the procedure.

Frequency refers to the repetition of the behaviour over a period of time (duration of observation). It is classified as intermittent when only one movement is observed in 10 s and as constant when ≥1 movements are observed in 10 s.
Resistance refers to the limitation in performing a passive movement on the anatomical region exhibiting the behaviour. Resistance is classified as mild-to-moderate for scores of 2–3 (out of 5) and as intense for scores of 4–5.

The RASS was used to determine the level of sedation. RASS scores range from −5 to −1, as follows: unarousable (−5), deep sedation (−4), moderate sedation (−3), light sedation (−2), and drowsy (−1).[29]

The GCS was used to assess the level of consciousness. Total scores on this 3-item scale (eye opening, verbal response, and motor response) range from 3 to 15 points, with lower scores indicating a lower level of consciousness. Based on the total number of points, consciousness impairment is classified as mild (14–15 points), moderate (9–13), or severe (3–8).[30]

We also registered the following variables: demographic characteristics, medical history, severity indicators, analgesia and sedation treatment (continuous or intermittent), neurological characteristics, ICU length of stay, and mortality.

2.5. Statistical analysis

We performed a descriptive analysis of the demographic and clinical characteristics and pain scores across the study time points, procedures, and measurement conditions.

To determine the discriminative ability of the ESCID-DC scale, adjusted for the level of sedation and consciousness, the AUC was calculated from the covariate-specific receiver operating characteristic curve estimated by the induced semiparametric method using the R-package "ROCRegression".[31] An AUC >0.7 indicates that the scale presents an acceptable discrimination capacity.[32]

To analyse differences in pain scores across the measurement conditions, a mixed-effect linear regression model was fitted. The response variable was the ESCID-DC score during the painful procedures. The fixed independent variables were procedure (tracheal suctioning, right nail bed pressure, and left nail bed pressure), baseline pain, level of consciousness, sedation level, and brain injury aetiology. The patient was included as a random variable.

The significance level was set at $\alpha = 0.05$. The R software v. 4.3.3 (R Core Team, 2024) was used to perform all statistical analyses.[33]

2.6. Ethical considerations

The study was approved by the Clinical Research Ethics Committees at the 17 participating hospitals (reference hospital approval code: 20/483). ClinicalTrials.gov: NCT04898491, available at: https://classic.clinicaltrials.gov/ct2/show/NCT04898491. This research study was conducted in accordance with all relevant Spanish and European Union legislation on data management and privacy. Written consent was obtained from the relatives of all patients included in the study.

3. Results

3.1. Clinical and demographic characteristics of the sample

A total of 418 patients were enrolled. Pain scores were obtained in 369 patients under deep sedation and in 346 patients under light-to-moderate sedation. In 293 patients, pain scores were obtained under both deep and light-to-moderate sedation (Fig. 1).

Table 2 shows the demographic and clinical characteristics of the sample. Most of the patients (68%) were men. The mean (standard deviation) age was 56.2 (16.3) years. The primary aetiology of the brain injury was vascular in 195 (46.7%) cases and trauma in 162 (38.8%) cases. Neurosurgery was required in 190 (45.5%) patients. Focal neurological signs were present in 200 (47.8%) patients.

Table 3 shows the level of consciousness and the therapeutic regimens for analgesia and sedation under the deep and light-to-moderate sedation. Overall, the level of consciousness in the sample was low, with a median GCS score <9 in both assessments. The most commonly administered analgesics in the continuous infusion regimen were opioids, which were administered to 327 (88.6%) patients in the first assessment (deep sedation) and 255 (65%) in the second one (light-to-moderate sedation). Paracetamol was the most commonly used analgesic administered in the discontinuous regimen (>30%).

3.2. Pain scores

Fig. 2 shows the distribution of ESCID-DC scores at the three time points and different procedures according to the level of sedation. As that figure shows, the pain score increased during painful procedures under both deep and light-to-moderate sedation. In most cases, the ESCID-DC score measured before and after the procedures was 0, indicating no behavioural response. Most scores obtained during the nonpainful procedure were 0.

3.3. Discriminative ability of the ESCID-DC

Fig. 3 shows the covariate-specific receiver operating characteristic curves, with the level of consciousness included as a covariate, for the two sedation levels and the three painful procedures. During tracheal suctioning, the ESCID-DC was highly discriminative, regardless of the level of consciousness or sedation (Fig. 3A and B). For patients with a GCS score of 4, the AUC was 0.89 (95% CI: 0.84–0.93) under deep sedation and 0.88 (95% CI: 0.84–0.94) under light-to-moderate sedation. In patients with higher levels of consciousness (GCS score = 8 and 12), the discriminative ability was nearly optimal, with AUC values of 0.99 (95% CI: 0.99–1) and 0.99 (95% CI: 0.98–1).

However, for the nail bed pressure procedures, the level of consciousness significantly impacted its discriminative performance, with discriminative ability increasing in line with GCS scores, both under deep (Fig. 3C and E) and light-to-moderate sedation (Fig. 3D and F). Under deep sedation, AUC values for the left and right nail bed procedures, respectively, increased from 0.66 (95% CI: 0.40–0.69) and 0.67 (95% CI: 0.42–0.70) for a GCS score of 4 to 0.96 (95% CI: 0.93–0.99) for a GCS score of 8. Under light-to-moderate sedation, AUC values rose from 0.65 (95% CI: 0.56–0.72) to 0.66 (95% CI: 0.58–0.73), respectively, for a GCS score of 4 to 0.96 (95% CI: 0.93–0.98) and for a GCS score of 12. For nail bed pressure procedures, a minimum GCS score of 5 was required to achieve adequate discrimination, with AUC values of 0.77 (95% CI: 0.70–0.80) (Fig. 3C); 0.71 (95% CI: 0.65–0.76) (Fig. 3D); 0.79 (95% CI: 0.72–0.81) (Fig. 3E); and 0.72 (95% CI: 0.66–0.77) (Fig. 3F).

3.4. Differences in ESCID-DC scores across the different conditions

Table 4 and Fig. 4 show the results of the mixed-effect regression model. Tracheal suctioning was the most painful procedure. However, the differences in pain levels between this procedure and right or left nail bed pressure depended on the level of consciousness. For patients with a GCS score of 4, the mean difference between tracheal suctioning and right nail bed pressure was 1.42 (95% CI: 0.663 to 2.176, $p < 0.001$). This difference became more pronounced with higher GCS scores, rising by 0.154 points (95% CI: 0.049–0.259, $p = 0.004$) for each one point increase in the GCS score (Table 4). No significant differences were observed between the two pressure procedures (mean difference = 0.207; 95% CI: −0.550–0.964, $p = 0.991$). Higher baseline pain levels were associated with higher mean ESCID-DC scores across all procedures (0.334; 95% CI: 0.163–0.506, $p < 0.001$, per unit increase).

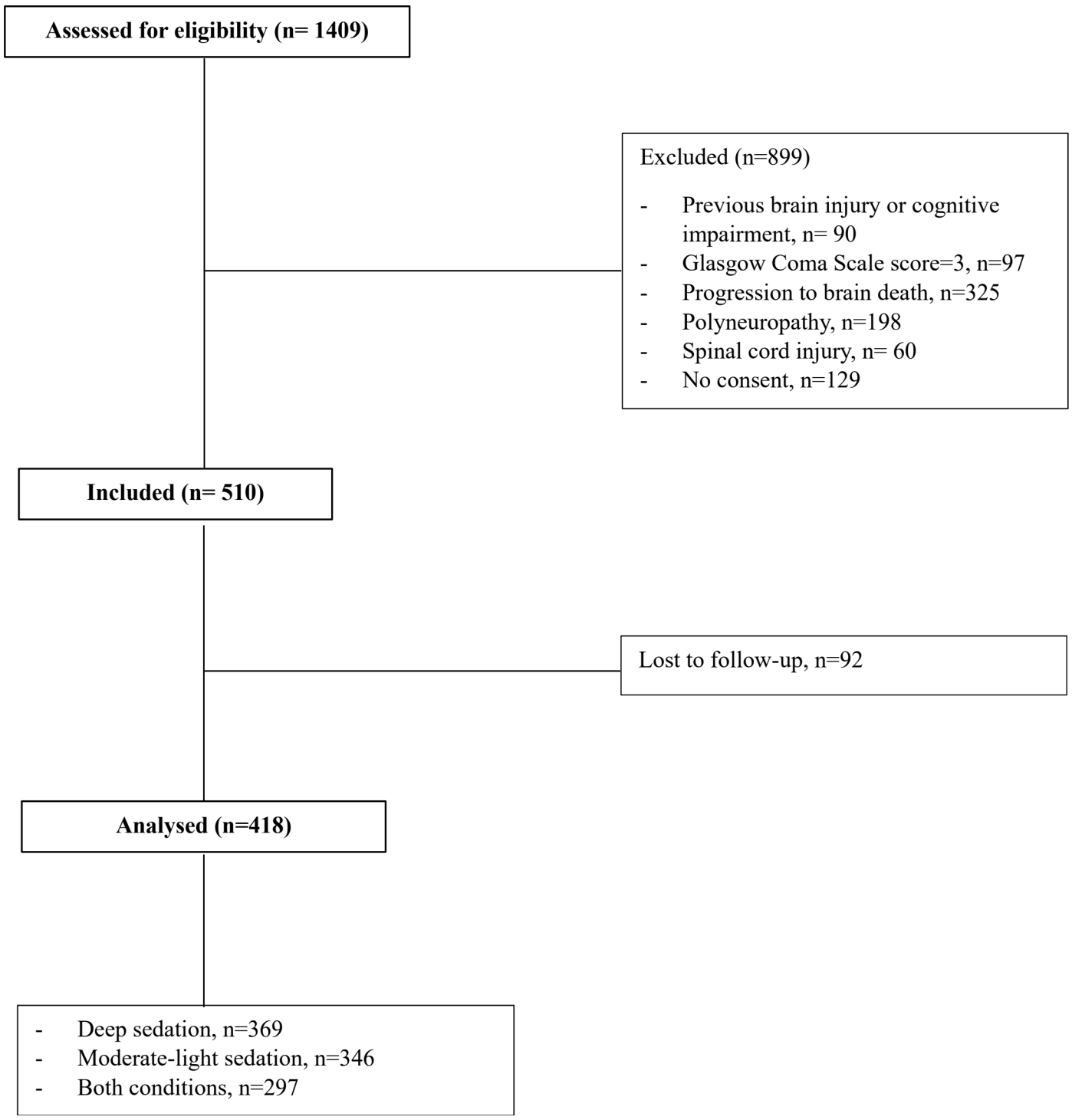

Fig. 1. Study flow chart.

Table 2
Sample characteristics (n = 418).

Characteristics	n (%)[a]
Age, mean (SD)	56.2 (16.3)
Sex, male	284 (68%)
Clinical history	
Chronic pain	35 (8.4%)
Chronic use of analgesics	40 (9.6%)
Psychotropic substance abuse	76 (18.2%)
Diabetes mellitus	53 (12.7%)
Simplified acute physiology Score II, median (IQR)	49.50 (37–62)
Brain injury aetiology	
Traumatic	162 (38.8%)
Vascular	195 (46.7%)
Other	61 (14.6)
Brain injury	
Focal/multifocal	360 (86.1%)
Diffuse	58 (13.9%)
Focal neurologic signs	200 (47.8%)
Neurosurgery	190 (45.5%)
Days in the ICU, median (IQR)	21 (11–32)
ICU mortality	56 (13.4%)

Abbreviations: ICU: intensive care unit; IQR: interquartile range; SD: standard deviation.

[a] All values given as n (%) unless otherwise indicated.

Mean scores under light-to-moderate sedation were nearly one point higher than those obtained under deep sedation (0.907; 95% CI: 0.638−1.175, $p < 0.001$) (Table 4). Fig. 4 illustrates the estimated marginal means for each sedation level, with a visual summary of group differences.

Brain injury was not included in the mixed model because we did not observe any significant association between this variable and the ESCID-DC score.

4. Discussion

To our knowledge, this is the first study to specifically assess the discriminative ability of a behavioural pain assessment tool (ESCID-DC) in patients with acquired brain injury under different levels of sedation and consciousness. Our results underscore the important influence of the level of consciousness on pain scores. We found that a minimum GCS score of 5 was needed to adequately discriminate pain during less painful or less intense procedures, regardless of the level of sedation. Procedure-related pain levels were higher in patients with baseline pain, suggesting the need for an individualised assessment of pain according to the presence or absence of basal pain.

Table 3
Level of consciousness, degree of sedation, and analgesic/sedation treatment administered on the day of pain assessment.

Variables	Deep sedation (n = 367)	Moderate-to-light sedation (n = 344)
Glasgow Coma Scale score, median (IQR); missing	5 (4, 7); 2	8.50 (7, 9); 2
Richmond Agitation-Sedation Scale score, median (IQR); missing	−4 (−4, −4); 2	−2 (−3, −2); 1
Continuous intravenous infusion[a], n (%)		
Fentanyl	133 (36)	91 (26.3)
Morphine	109 (29.5)	81 (23.4)
Remifentanil	85 (23)	53 (15.31)
Propofol	245 (66.4)	117 (33.8)
Midazolam	64 (17.3)	16 (4.6%)
Dexmedetomidine	32 (8.6)	40 (11.5)
Intravenous push administration[b], n (%)		
Fentanyl	46 (12.4)	28 (8)
Paracetamol	119 (32.2)	137 (39.6)
Metamizole	52 (14)	73 (21)
Dexketoprofen	13 (3.5)	19 (5.5)
Midazolam	36 (9.7)	14 (4)
Preemptive analgesia prior to initiation of procedures, n (%)		
< 1 h	36 (9.7)	55 (15.9)
1–8 h	187 (50.6)	202 (58.3)
Days between ICU admission and study enrolment, median (IQR)	3 (1–7)	7 (3–13)

Abbreviations: ICU: intensive care unit; IQR: interquartile range.
[a] Continuous intravenous infusion administered 24 h before pain assessment.
[b] Intravenous push infusion administered up to 8 h prior to pain assessment.

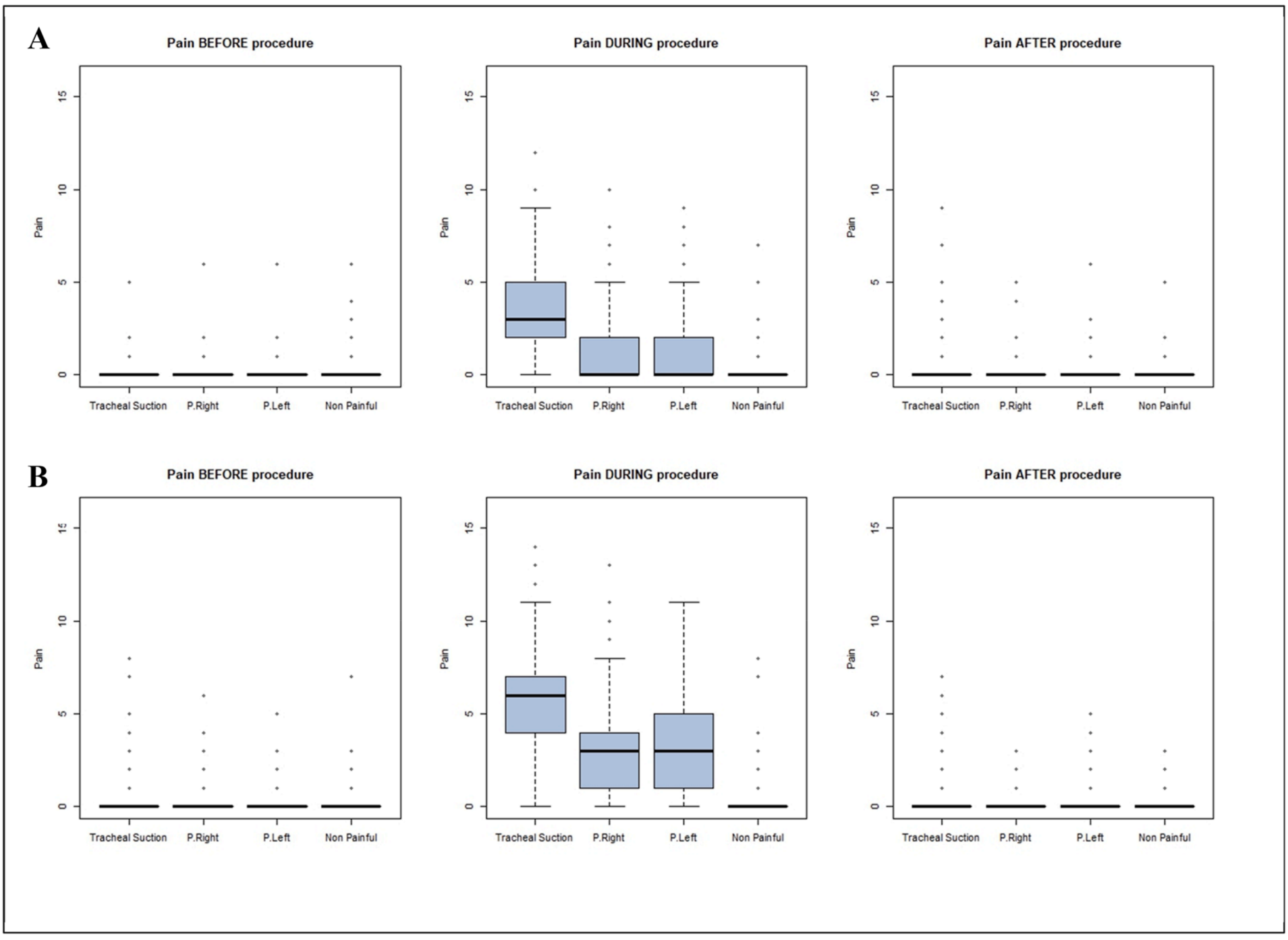

Fig. 2. ESCID-DC scores according to procedure type, time point, and sedation level: A) Pain scores under deep sedation (RASS score: -4); B) Pain scores under moderate-to-light sedation (RASS score: -3, −2). ESCID-DC: Escala de Conductas Indicadoras de Dolor-Daño Cerebral; RASS: Richmond Agitation-Sedation Scale.

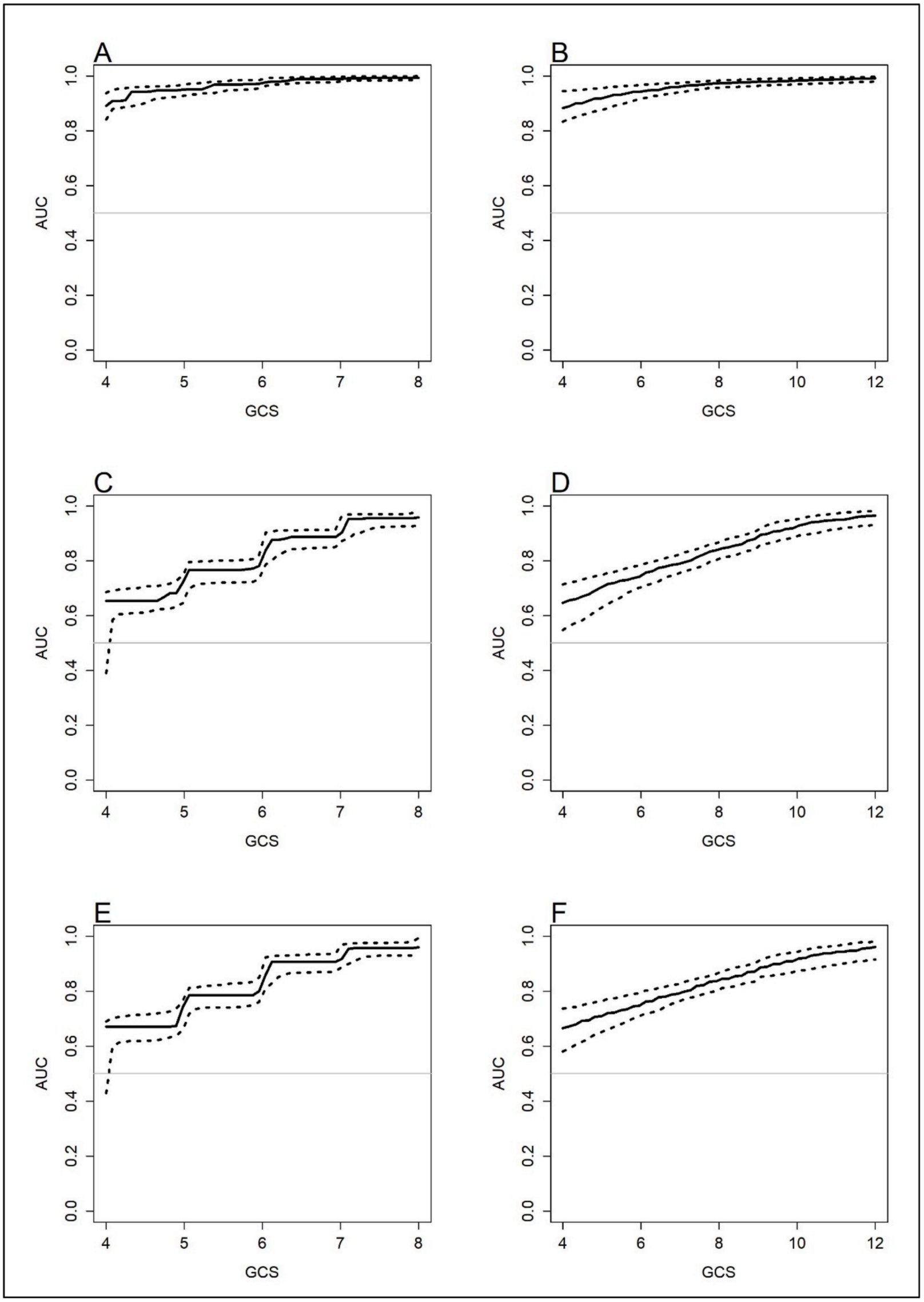

Fig. 3. Area under the curve (AUC) values from covariate-specific ROC curves according to the level of consciousness, sedation level (deep vs. moderate-to-light), and the three painful procedures: A) Tracheal suctioning under deep sedation (RASS score: −4); B) Tracheal suctioning under moderate-to-light sedation (RASS score: −3, −2); C) Right nail bed pressure under deep sedation (RASS score: −4); D) Right nail bed pressure under moderate-to-light sedation (RASS score: −3, −2); E) Left nail bed pressure under deep sedation (RASS score: −4); and F) Left nail bed pressure under moderate-to-light sedation (RASS score: −3, −2). The solid line represents the AUC, while the dashed lines indicate the corresponding 95% confidence intervals. GCS: Glasgow Coma Scale; RASS: Richmond Agitation-Sedation Scale; ROC: receiver operating characteristic.

Table 4
Mean differences compared to reference in ESCID-DC scores obtained from a mixed-effect linear regression model where procedure, level of consciousness, baseline pain, degree of sedation, and interaction between procedure and level of consciousness were included as independent variables.

Effect (n = 293)	Mean difference	95% CI	p value
Left nail bed pressure[a]	0.207	(-0.550, 0.964)	0.591
Tracheal suctioning[a]	1.420	(0.663, 2.176)	<0.001
GCS score (per unit increase)	0.347	(0.248, 0.446)	<0.001
Baseline pain[b] (per unit increase)	0.334	(0.163, 0.506)	<0.001
Light-moderate sedation[c]	0.907	(0.638, 1.175)	<0.001
Left nail bed pressure: GCS	0.001	(-0.104, 0.106)	0.991
Tracheal suctioning: GCS	0.154	(0.049, 0.259)	0.004

Abbreviations: CI: confidence interval; ESCID-DC: Escala de Conductas Indicadoras de Dolor-Daño Cerebral; GCS: Glasgow Coma Scale.
[a] Compared to pressure right nail bed.
[b] Pain present prior to initiating the procedures.
[c] Compared to deep sedation.

Patients admitted to the ICU are highly heterogeneous in terms of their clinical characteristics. In patients unable to self-report, behavioural pain assessment tools require precise, case-specific interpretation. Behavioural scales such as the ESCID-DC may lead to subjective clinical assessments, and thus, the results may vary depending on the training, experience, and skills of the evaluating clinician. It is essential that professionals receive proper training and instruction before using behavioural tools to ensure accurate and reliable assessments. For this reason, it is important to clearly define the optimal conditions for using these tools.[34] To accurately assess pain in patients with acquired brain injury and disorders of consciousness, it is important to use scales that have been validated in this specific population. Before performing a pain assessment, it is crucial to consider both the level of consciousness and degree of sedation to ensure that the patient's motor function is sufficient to obtain an observable behavioural response. In patients who exhibit pain behaviours at baseline, an analgesia trial should be conducted before performing care-related procedures. If the pain behaviour decreases or disappears following administration of analgesics, then this would confirm the presence of baseline pain.[16,23] That said, it may be difficult or even impossible to perform an analgesia trial in patients requiring an urgent procedure.

Focal neurological signs secondary to brain injury are common in this population. However, the presence of this sign does not rule out the presence of pain in patients without any obvious behavioural indicators of pain or who show only a weak behavioural response.[22]

In contrast to previous studies, the overall level of consciousness in our sample was low (median GCS score <9) for both measurement conditions. In the study by Gélinas et al. (n = 226),[35] consciousness was only mildly impaired (GCS score = 13–15) in more than half of the sample (56%) and only 16% had severe impairment (GCS score <9), which explains the lighter sedation level in that study (RASS score: -1 [interquartile range {IQR}: -4, +3]). By contrast, the level of consciousness in the study by Bernard et al.[24] was similar to that observed in our cohort (GCS score = 5 [IQR: 4, 7]) with a median RASS score of −3 (IQR: −4, −2). For this reason, it is more appropriate to compare our results to the findings reported in the latter study.

In the literature, comparative data on the impact of different levels of sedation on pain behaviours are scant. Although some studies have shown that the behavioural response to pain decreases in line with the level of sedation,[18,36] the impact of sedation on the discriminative ability of behavioural pain scales has not been explored in detail. In this study, the ability of the ESCID-DC to discriminate pain did not depend on the level of sedation but rather on the level of consciousness and the intensity of the

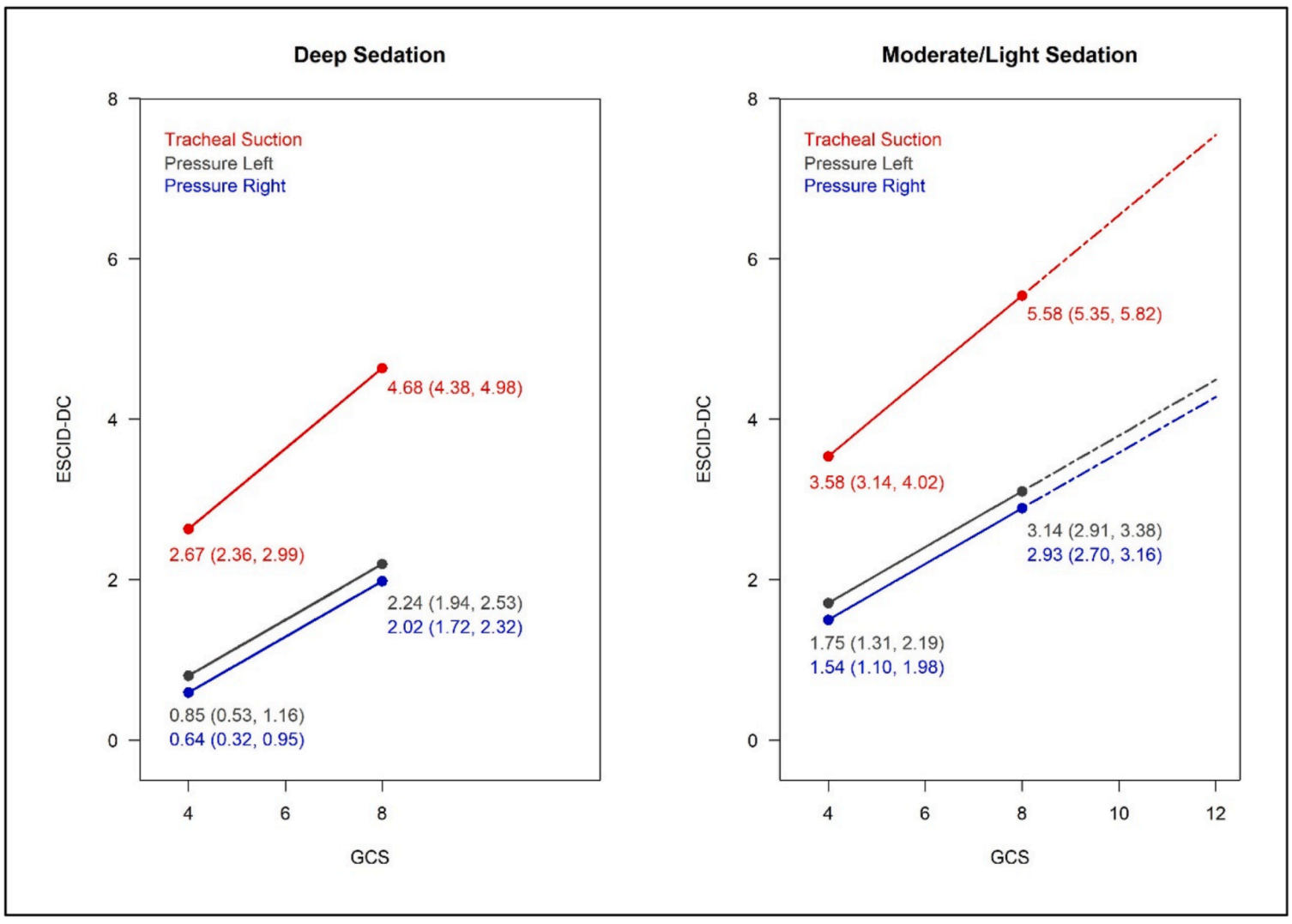

Fig. 4. Estimated marginal mean ESCID-DC scores obtained from the mixed-effect linear model, for each procedure, adjusted by level of consciousness, degree of sedation, and interaction between procedure and level of consciousness. Pain scores increase in line with higher Glasgow Coma Scale (GCS) scores, especially during tracheal suctioning. On average, the ESCID-DC score is close to one point higher under moderate-to-light sedation than under deep sedation. The points represent the mean values with 95% confidence intervals. ESCID-DC: Escala de Conductas Indicadoras de Dolor-Daño Cerebral.

procedure; consequently, during the pressure procedures, a minimum GCS score of 5 was required to ensure adequate discrimination (AUC > 0.7), regardless of the level of sedation. By contrast, during tracheal suctioning, discrimination was acceptable at all levels of consciousness and at both levels of sedation, a finding consistent with previous reports that have found that painful stimuli generate more evident behavioural responses, even in patients with a lower level of consciousness.[18]

In our sample, pain assessment was performed a median of 4 days earlier in patients under deep sedation versus those under light-to-moderate sedation. This finding is important because it suggests that it may be feasible to assess pain sooner after ICU admission as long as the minimum GCS value (≥5) is met.

Not surprisingly, ESCID-DC scores were lower under deep sedation than under light-to-moderate sedation. Despite this lower behavioural response to pain under deep sedation, several experts have warned that the number of observed pain behaviours does not necessarily indicate the pain intensity.[17,23,37] One of the strengths of the ESCID-DC is the inclusion of four items to assess facial expression, which permits the detection of behavioural responses in patients whose bodily response to pain is limited or even completely absent due to sedation. In the validation study of the Critical-Care Pain Observation Tool-Neuro, facial expression also emerged as the most commonly observed indicator of pain.[35]

Given that the behavioural response to pain may be attenuated in patients under deep sedation, it is essential to explore complementary strategies to better assess pain in these patients. In this regard, future studies could incorporate the use of advanced technical tools such as pupillometry, which has proven to be a promising alternative for detecting pain response in patients with disorders of consciousness.[38–41] The addition of such tools could further enhance the accuracy of pain assessment in patients with minimal behavioural expression, which in turn could help to optimise the analgesic regimen, thus avoiding unnecessary sedation in these patients.[22]

4.1. Limitations

This study has several limitations. First, the administration of analgesia prior to performing the procedures was not predetermined and we did not assess the effects of preprocedural analgesia, which could have provided relevant information with regards to the presence of baseline pain and its impact on subsequent pain assessments. Another limitation is that we only evaluated a limited number of painful procedures (tracheal suctioning and nail bed pressure). Including a broader range of clinical procedures would have allowed for a more complete evaluation of the interaction between level of consciousness, sedation, and type of procedure on behavioural indicators of pain. Finally, it was not possible to confirm the patient's experience of pain, mainly due to the low level of consciousness, which made it impossible in most cases to obtain self-reported data. In addition, we did not include proxy reporters (e.g., family members), even though this could have provided valuable information. Despite these limitations, a key strength of the study is its multicentre design, which makes the findings generalisable to a wide range of clinical settings. Another important strength is the systematic evaluation of the ESCID-DC at two different levels of sedation, which provides valuable evidence on the applicability of this scale in patients with acquired brain injury.

5. Conclusion

This study shows that several variables, including the level of consciousness and type of procedure, influence the discriminative ability of the ESCID-DC. In the less painful, less intense procedures (i.e., nail bed pressure), the scale required a GCS score ≥5 to adequately discriminate pain, regardless of the level of sedation. By contrast, during the more painful, more intense procedure (tracheal suctioning), the discriminative ability of the ESCID-DC was good at both levels of sedation, regardless of the GCS score.

This study also shows that ESCID-DC scores vary according to the type of procedure and the time of assessment. As expected, tracheal suctioning was associated with higher pain scores and nail bed pressure with lower scores. Importantly, the presence of baseline pain was associated with higher procedure-related pain scores. Pain scores were higher in patients under light-to-moderate sedation than in those under deep sedation, a finding that underscores the importance of considering the level of sedation when interpreting behavioural responses to pain.

The findings reported here are highly relevant as they can be used to better optimise pain monitoring in patients with acquired brain injury and to improve clinical decision-making based on sedation and consciousness levels.

CRediT authorship contribution statement

Candelas López-López, Gemma Robleda-Font, Ignacio Latorre-Marco, Montserrat Solís-Muñoz, María Carmen Sarabia-Cobo, Antonio Arranz-Esteban: Conceptualisation, Methodology, Funding acquisition, Supervision, Writing, review & editing.

Francisco Paredes-Garza, Aaron Castanera-Duro, Mónica Bragado-León, Emilia Romero de-San-Pío, Isabel Gil-Saaf, David Alonso-Crespo, Carolina Rojas-Ballines, María Teresa Pulido-Martos, Isabel Martínez-Yegles: Investigation, Project administration, Validation, Writing, review & editing.

Teresa Pérez-Pérez: Conceptualisation, Methodology, Supervision, Software, Formal analysis, Writing review & editing.

All authors have read and approve the final version of this manuscript.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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