

Using Pupillary Pain Index to Assess Nociception in Sedated Critically Ill Patients

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BACKGROUND: Pupillary reflex dilation is a reliable indicator of response to noxious stimulation. In a proof of concept study, we investigated the performance of pupillary pain index, a new score derived from pupillary reflex dilation measurements, to predict nociceptive response to endotracheal suctioning in sedated critically ill patients.

METHODS: Twenty brain-injured and 20 non-brain-injured patients were studied within 48 hours of admission (T1) in the intensive care unit and at 48–72 hours later (T2). Video-based pupillometer was used to determine pupillary reflex dilation during tetanic stimulation. The tetanic stimulation (100 Hz) was applied to the skin area innervated by the ulnar nerve and was stepwise increased from 10 to 60 mA until pupil size had increased by 13% compared to baseline. The maximum intensity value allowed the determination of a pupillary pain index score ranging from 1 (no nociception) to 9 (high nociception). The Behavioral Pain Scale response to endotracheal suctioning was measured thereafter.

RESULTS: Behavioral Pain Scale responses to endotracheal suctioning and pupillary pain index scores were positively correlated at T1 and T2 (both $P < .01$). After adjustments for repeated measurements and group of patients, the area under the receiver operating characteristic curve of pupillary pain index to predict Behavioral Pain Scale response to endotracheal suctioning was 0.862 (95% CI, 0.714–0.954). In the combined set of patients, a pupillary pain index score of ≤ 4 could predict no nociceptive response to endotracheal suctioning with a sensitivity of 88% (95% CI, 68%–97%) and a specificity of 79% (95% CI, 66%–88%). By contrast with endotracheal suctioning, tetanic stimulation had no effect on intracranial pressure in the brain-injured group.

CONCLUSIONS: These results are a proof of concept. The nociceptive response to endotracheal suctioning could be accurately predicted using the determination of pupillary pain index score in sedated critically ill patients whether they have brain injury or not. (Anesth Analg XXX;XXX:00–00)

KEY POINTS

- **Question:** Can nociception be assessed using measurements of pupillary reflex dilation in sedated critically ill patients?
- **Findings:** A new score, pupillary pain index, derived from pupillary reflex dilation, accurately predicted the subsequent Behavioral Pain Scale responses to endotracheal suctioning in brain-injured and non-brain-injured patients.
- **Meaning:** Pupillary pain index score could be used to assess nociception in sedated critically ill patients whether they have brain injury or not.

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Patients in the intensive care unit may experience pain that is recognized as one most bothersome experience.¹ Insufficient analgesia contributes to patient suffering and may cause agitation. Conversely, excessive use of opioids is associated with several side effects. Clinical pain scales, that is, the Behavioral Pain Scale and the Critical Care Pain Observation Tool, are recommended in the 2013 practice guidelines for noncommunicative intensive care unit patients.² The use of these clinical instruments was tested in brain-injured patients as well.^{3,4} However, dosing of hypnotics and/or severity of brain injury might have an impact on the performance of these clinical pain instruments in critically ill patients.^{5–7} In addition, physiological responses to noxious procedures may raise intracranial pressure (ICP) that could be deleterious in brain-injured patients with reduced intracranial compliance.⁸

Recent interest surrounds the use of video pupillometry in anesthesia and critical care.⁹ Portable infrared pupillometry can measure pupil size and 2 pupillary reflexes: pupillary light reflex to explore the integrity of midbrain function

and pupil reflex dilation amplitude in response to noxious stimulus, for example, tetanic stimulation applied to the skin area innervated by a sensorial nerve, skin incision, turning, or endotracheal suctioning. While pupillary light reflex was explored using quantitative pupillometry in critically ill patients,^{10–13} no data exist on the usefulness of pupil reflex dilation to explore nociception in this population.

In a proof of concept study, we measured the nociception during 2 successive noxious stimuli in sedated critically ill patients: tetanic stimulation and endotracheal suctioning. Tetanic stimulation was used as a standardized noxious stimulus to determine the pupillary pain index, a proposed new score derived from pupil reflex dilation measurements. Pupillary pain index overcomes the poor tolerance induced by using a predefined intensity of electric stimulation to get pupil reflex dilation in sedated intensive care unit patients.¹⁴ The objective of this study was to investigate the diagnostic performance of pupillary pain index in assessing nociception and predicting Behavioral Pain Scale response to endotracheal suctioning. We collected data from brain-injured and non-brain-injured sedated patients at 2 times to assess the reproducibility of pupillary pain index measurements. We hypothesized that pupillary pain index measurements could accurately predict nociceptive reactions to endotracheal suctioning in critically ill patients whether they had brain injury or not.

METHODS

This prospective observational study was conducted between April 2012 and September 2015 with the successive participation of 2 intensive care units of Grenoble University Hospital: 1 surgical intensive care unit and 1 neurointensive care unit. The institutional review board of Sud-Est II (Chairperson Prof. M David, Edouard Herriot Hospital, 69437, Lyon, France) approved the study design on April 4, 2012 (Ref 2012-009-2) and, given its observational nature, waived the requirement for written informed consent from relatives of each patient. The study protocol was registered with Clinicaltrials.gov (NCT02843893). This manuscript adheres to the applicable Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Participants

Patients were included if they were ≥ 18 years of age and required mechanical ventilation and sedation/analgesia using continuous infusion of hypnotics and opioids for a foreseeable period of ≥ 72 hours. Patients were not included if they had quadriplegia, were receiving concurrent treatment with neuromuscular blocking drugs, or they had unreactive bilateral mydriasis, refractory intracranial hypertension, imminent death within the first 12 hours or a known ocular pathology, or if a relative opposed to their participating in the study. They were also not included if they presented conditions or were receiving treatment known to alter pupil reflex dilation measurements, that is, diabetic retinopathy, amyloidosis, or treatment with droperidol, clonidine, or metoclopramide.

Patients were admitted to the intensive care unit after either moderate-to-severe brain injury (brain-injured group) as defined by an initial Glasgow Coma Scale score of 3–13 or other severe organ dysfunction(s) (non-brain-injured group) and were managed according to the international

guidelines for sedation and analgesia.^{2,15} Patients received continuous IV infusions of midazolam or propofol, sufentanil, and ketamine at the discretion of the physician in charge. Sedation and analgesia levels were measured every 4 hours using the Richmond Agitation-Sedation Scale and the Behavioral Pain Scale, respectively, with an objective of Richmond Agitation-Sedation Scale ≤ 5 and Behavioral Pain Scale 3 at baseline.

Patients were mechanically ventilated to maintain normocapnia and normoxia. They were maintained under normothermia (36°C–37°C). An intraparenchymal device (Codman Microsensors ICP transducers; Johnson Johnson, Issy-les-Moulineaux, France; and Sophysa Pressio; Sophysa, Orsay, France) was used for continuous measurement of ICP in the brain-injured group to maintain ICP below 20 mmHg and cerebral perfusion pressure between 60 and 70 mmHg via vasoactive support with norepinephrine and, if needed, plasma volume expansion with crystalloids.

Data Sources/Measurements

Measurements were taken within 48 hours of admission to the intensive care unit in patients who were stable, sedated, and mechanically ventilated (T1) and were repeated at 48–72 hours later during the same conditions (T2). Pupillary measurements were performed where endotracheal suctioning was required at T1 and T2 according to the following order: pupillary pain index measurement during tetanic stimulation, then Behavioral Pain Scale measurements at rest and during endotracheal suctioning with concomitant pupil size measurements to determine pupil reflex dilation measurements (Figure 1). The Richmond Agitation-Sedation Scale and Behavioral Pain Scale assessments were performed immediately after pupil reflex dilation measurements by the in-charge nurse blinded to the pupillary measurements.

A portable infrared pupillometer (Algiscan; IdMed, Marseille, France) was used to measure baseline pupil size (mm) and the variation of the pupillary surface (pupil reflex dilation amplitude, in %) in response to 2 noxious stimuli: endotracheal suctioning and tetanic stimulation. The tetanic stimulation (100 Hz) was applied to the skin area innervated by the ulnar nerve of the forearm, and the intensity of electric stimulation automatically increased in stepwise increments of 10 mA every second, from 10 to 60 mA, until pupil size had increased by $\geq 13\%$ compared to baseline. Once the threshold of 13% is reached, electrical stimulation is automatically stopped. This threshold value was based

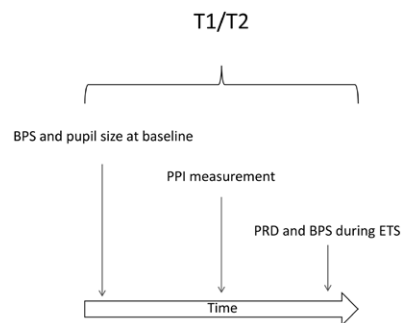


Figure 1. Timeline for BPS and pupil size measurements at T1 and T2. BPS indicates Behavioral Pain Scale; ETS, endotracheal suctioning; PPI, pupillary pain index; PRD, pupil reflex dilation.

from previous studies¹⁶⁻¹⁸ where pupil reflex dilation amplitude between 13% and 25% from baseline was large enough to reflect a pupil reaction to noxious stimulation with no other physiological reactions to noxious stimulation such as tachycardia, arterial hypertension, eye weeping, or sweating. The maximum intensity value allowed the determination of a pupillary pain index score ranging from 1 (pupil reflex dilation <5% for 60 mA during 3-second stimulation, no nociception) to 9 (pupil reflex dilation >13% for 10 mA during 1-second stimulation, high nociception)¹⁹ (Table 1). In the brain-injured group, pupillary pain index score was obtained from the 2 eyes during right and left forearm noxious stimulations, that is, 4 measures in total, to account for a possible impact of focal neurological damage. A 5-minute washout period was allowed between each pupillary pain index measurement. The highest pupillary pain index score was taken for the analysis. In the non-brain-injured group, one pupillary pain index measurement was obtained from either eye regardless of stimulated forearm. In addition, pupillary light reflex was measured in the brain-injured group to ensure the integrity of neurological function. Pupillary light reflex amplitude was expressed as a percentage of pupil size change from baseline in response to a calibrated light stimulation (320 lux, 1 second).

Variables included patient characteristics, Simplified Acute Physiology Score II, Richmond Agitation-Sedation Scale, heart rate (HR), blood pressure, ICP, pupil size, and Behavioral Pain Scale scores. Used sedative and opioid doses were also recorded.

Statistical Analysis

Continuous variables are expressed as median and interquartile range (25–75th percentile) unless stated otherwise. Comparisons between the 2 groups used nonparametric Mann–Whitney test, χ^2 test, or Fisher exact test. Correlation between physiological variables, that is, pupillary pain index score, HR, and systolic blood pressure measurements during tetanic stimulation, and Behavioral Pain Scale responses to endotracheal suctioning used the Spearman rank coefficient. Statistical significance was declared when $P < .05$ (Stata version 13.0; Stata Corp, College Station, TX).

Electrical Intensity (mA) to Increase Pupil Size by $\geq 13\%$ to Baseline	Corresponding Pupillary Pain Index Score
10	9
20	8
30	7
40	6
50	5
60	4
60	3
60	2
Pupil size increasing less of 5%	1

Tetanic stimulation (100 Hz) is increased in stepwise increments of 10 mA every second. The pupillary pain index score of 4, 3, and 2 corresponds to the duration of 60-mA electrical stimulation of 1, 2, or 3 seconds, respectively.

Based on a Behavioral Pain Scale score of ≥ 5 being able to predict significant pain during nociceptive procedures,² the Behavioral Pain Scale responses to endotracheal suctioning were dichotomized into 2 categories: no or mild reaction to pain (ie, Behavioral Pain Scale 3–4) and moderate-to-high reaction to pain (ie, Behavioral Pain Scale ≥ 5). The diagnostic performance of the pupillary pain index scores at correctly classifying Behavioral Pain Scale responses to endotracheal suctioning at T1 and at T2 was evaluated using the area under the receiver operating characteristic curve (95% CI). The area under the receiver operating characteristic curves of T1 and T2 were compared using a test for dependent receiver operating characteristic curves (same sample).²⁰ We calculated a combined area under the receiver operating characteristic curve of the 2 groups of patients. To account for the fact that the 2 populations might have different pupillary pain indices, we stratified the distribution of pupillary pain index on the brain status. We computed the CI on the area under the receiver operating characteristic curve by bias-corrected bootstrap. To account for the repetition of measures for each patient, we clustered the bootstrap by patient. This method assumes a common discriminative performance of pupillary pain index score for the 2 populations.²¹ The best cutoff value of pupillary pain index score was determined according to the maximization of both sensitivity and specificity.²² Because this study was a proof of concept, the needed population size was not previously estimated. A convenience sample of >30 sedated critically ill patients was then decided as recommended in pilot studies.

RESULTS

There were 51 enrolled patients. Of these, 40 patients were retained in the analysis because 11 had important missing data, for example, incorrect order or excessive delay between pupillary pain index measurement and Behavioral Pain Scale measurements at rest and during endotracheal suctioning, or no measurements at T2. The study included 20 brain-injured and 20 non-brain-injured patients (Table 2). Patients in the brain-injured group had suffered a traumatic brain injury ($n = 11$), stroke ($n = 7$), or subarachnoid hemorrhage ($n = 2$). Their initial Glasgow Coma Scale score was 10 (7–13), and their pupillary light reflex amplitude was 13% (9–18) and 18% (9–23) at T1 and T2, respectively. They were primarily sedated with midazolam and sufentanil. Patients in the non-brain-injured group had suffered multiple trauma ($n = 9$), sepsis ($n = 6$), postoperative complications ($n = 2$), or other ($n = 3$). They received propofol and sufentanil. Using these sedation/analgesia regimens, the 2 groups of patients were equally unresponsive at baseline with median Richmond Agitation-Sedation Scale scores of -5 and median Behavioral Pain Scale scores of 3. The doses of sufentanil were higher in the brain-injured group than in the non-brain-injured group. As expected, the duration of mechanical ventilation and the length of intensive care unit stay were longer in the brain-injured group. No changes in the doses of sufentanil were found between T1 and T2 in either group of patients (data not shown).

In the 2 groups of patients, pupil reflex dilation measurements during endotracheal suctioning were positively correlated with concomitant Behavioral Pain Scale scores at T1 (Spearman coefficient = 0.66; $P < .01$) and T2 (Spearman

Table 2. Characteristics of the Brain-Injured Patients (n = 20) and Non-Brain-Injured Patients (n = 20)

Variables	Brain Injured	Non-Brain Injured	P Value
Age, y	48 (39–60)	52 (43–60)	.43
Sex, male/female, n	17/3	18/2	.63
Body mass index	23 (22–25)	24 (22–26)	.82
Simplified Acute Physiology Score II	42 (36–50)	37 (33–48)	.33
HR, /min	76 (68–85)	85 (77–113)	.02
SBP, mmHg	130 (124–140)	108 (103–124)	<.01
Richmond Agitation-Sedation Scale	–5 (–5 to –4)	–5 (–5 to –4)	.22
Behavioral pain scale at baseline	3 (3–3)	3 (3–3)	.46
Propofol, n	1	16	...
Dose, mg/kg/h	2.4	2.4 (1.7–3.8)	...
Midazolam, n	19	4	...
Dose, mg/kg/h	0.11 (0.09–0.14)	0.08 (0.08–0.09)	...
Ketamine, n	9	0	...
Dose, mg/kg/h	2.0 (1.6–2.7)
Sufentanil, n	20	20	...
Dose, µg/kg/h	0.57 (0.49–0.68)	0.44 (0.24–0.62)	.02
Mechanical ventilation duration, d	16 (11–20)	6 (4–14)	<.01
Length of intensive care unit stay, d	23 (17–30)	9 (5–21)	<.01

Variables were measured at baseline within 48 h of admission (T1). Data are expressed as median (25–75th percentile) unless otherwise specified. Abbreviations: HR, heart rate; SBP, systolic blood pressure.

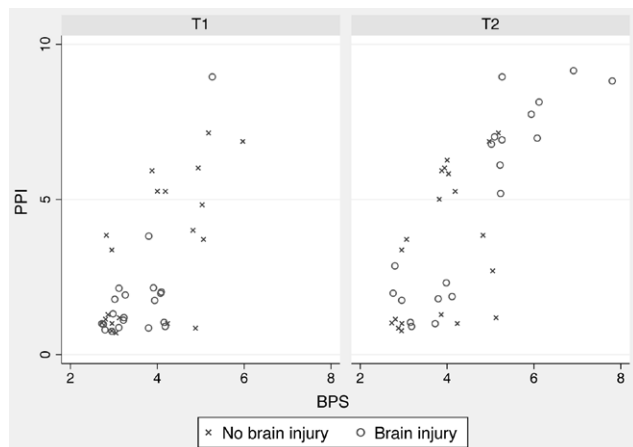


Figure 2. Individual PPI scores and BPS responses to endotracheal suctioning in the 40 critically ill sedated patients at 2 different times of their stay in the intensive care unit: T1 (left) and T2 (right). Individual data are circles (brain-injured patients) and crosses (non-brain-injured patients). Due to tied values, random noise was used to show all 40 measurements. BPS indicates Behavioral Pain Scale; PPI, pupillary pain index.

coefficient = 0.78; $P < .01$). In addition, the pupillary pain index measurements during tetanic stimulation were positively correlated with Behavioral Pain Scale responses to endotracheal suctioning at T1 (Spearman coefficient = 0.64; $P < .01$) and T2 (Spearman coefficient = 0.76; $P < .01$) (Figure 2). No significant correlation was found between pupillary pain index scores and physiological responses to tetanic stimulation such as HR (Spearman coefficient = 0.20) and systolic blood pressure (Spearman coefficient = 0.25).

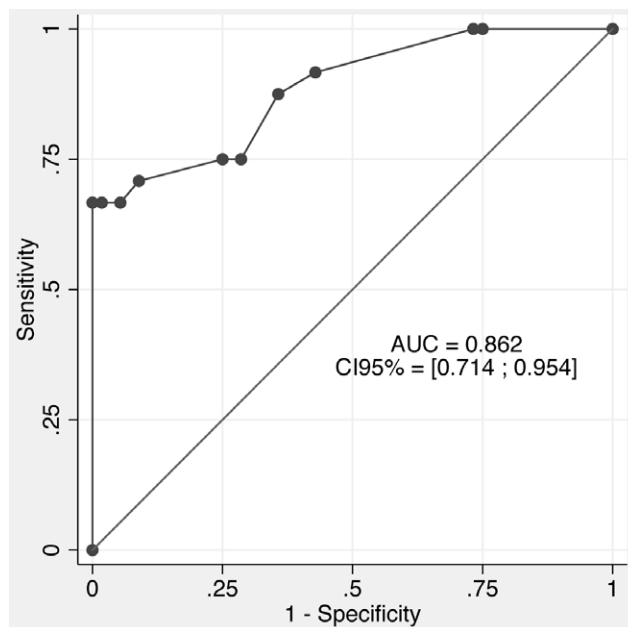


Figure 3. Receiver operating characteristic curve of the pupillary pain index in the 40 critically ill sedated patients. AUC indicates area under the curve.

Endotracheal suctioning elicited 56 responses with Behavioral Pain Scale 3–4 and 24 with Behavioral Pain Scale ≥ 5 . As expected, Behavioral Pain Scale 3–4 had significantly lower pupillary pain index scores than Behavioral Pain Scale ≥ 5 : 1 (1–3) vs 7 (5–8), respectively ($P < .01$). With regards to the diagnostic performance of pupillary pain index to predict Behavioral Pain Scale response during endotracheal suctioning, the corresponding area under the receiver operating characteristic curve was 0.871 (95% CI, 0.700–1.000) at T1 and 0.894 (95% CI, 0.783–1.000) at T2. Because there was no difference in the 2 area under the receiver operating characteristic curves between T1 and T2 ($P = .822$), a global area under the receiver operating characteristic curve was constructed: 0.862 (95% CI, 0.714–0.954) (Figure 3). The best cutoff value to predict a Behavioral Pain Scale response to endotracheal suctioning of 3–4 was a pupillary pain index score of ≤ 4 with a sensitivity of 88% (95% CI, 68%–97%) and a specificity of 79% (95% CI, 66%–88%). The positive and negative predictive values were 64% and 94%, respectively.

Pupil size at baseline was comparable at T1 and T2 between the 2 groups of patients: 2.1 mm (2.0–2.3) in the brain-injured group versus 2.3 mm (2.2–2.7) in the non-brain-injured group ($P = .147$). Pupil reflex dilation measurements in the 2 groups were comparable: 8% (3–26) vs 12% (3–27), respectively ($P = .490$). In the brain-injured group, the pupillary pain index scores during right and left forearm noxious stimulations were similar: 1 (1–2) vs 1 (1–2), respectively ($P = .484$). In this group, a pupillary pain index score of ≤ 3 had a sensitivity of 100% (95% CI, 73%–100%) and a specificity of 96% (95% CI, 82%–99%) to predict a Behavioral Pain Scale response to endotracheal suctioning of 3–4. In addition, endotracheal suctioning resulted in a significant rise in ICP while tetanic stimulation had no impact on ICP: 15 mmHg (10–17) at baseline versus 20 mmHg (15–22) during endotracheal suctioning ($P < .01$) and

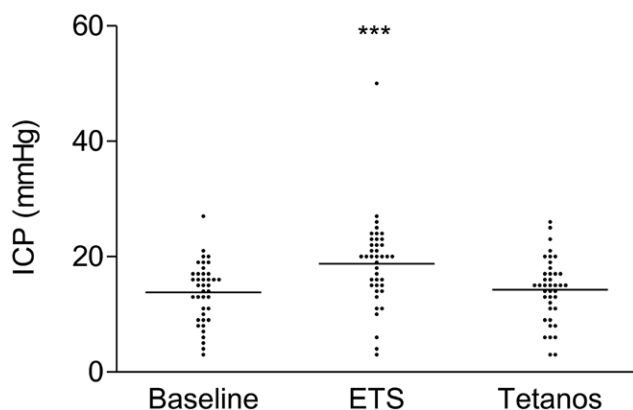


Figure 4. Individual effects and median values of ETS and tetanic stimulation as noxious stimuli on ICP in the group of brain-injured patients (n = 20 patients). *** $P < .01$ versus baseline. ETS indicates endotracheal suctioning; ICP, intracranial pressure.

15 mmHg (11–17) during pupillary pain index measurements (Figure 4). There were 12 patients and 3 patients who raised their ICP at ≥ 20 mmHg during endotracheal suctioning and tetanic stimulations, respectively.

DISCUSSION

Our results are a proof of concept and indicate that nociception could be reliably and safely assessed using quantitative pupillometry in sedated critically ill patients whether they had brain injury or not. A low pupillary pain index score accurately and repeatedly predicted the absence of nociception during endotracheal suctioning taken as a standardized noxious stimulus. In addition, tetanic stimulation to determine pupillary pain index score had no impact on ICP in brain-injured patients.

We investigated quantitative pupillometry and pupillary pain index score as a potential tool to assess nociception in critically ill sedated patients. During general anesthesia, pupil reflex dilation has shown greater sensitivity when compared with other variables used to assess response to noxious stimulation, such as HR and arterial blood pressure.^{23,24} We previously found marked differences in pupil reflex dilation measurements during tetanic stimulation of the 2 legs according to whether the stimulated leg was under unilateral popliteal sciatic nerve blockade or not in anesthetized patients.¹⁷ In anesthetized women, pupil reflex dilation amplitude evoked by a tetanic stimulation has been shown to be as accurate as remifentanyl effect-site concentration to predict movement response on cervical dilation.¹⁸ In major gynecologic surgery, reduced intraoperative remifentanyl consumption and postoperative morphine requirements were found where analgesia was guided by pupil reflex dilation measurements.²⁵ In sedated non-brain-injured intensive care unit patients, pupil reflex dilation unambiguously distinguished between noxious and non-noxious procedures²⁶ and was used to predict autonomic response after endotracheal suctioning.¹⁴ Collectively, these findings indicate that pupil reflex dilation might be an appropriate candidate to explore response to a noxious stimulation in critically ill sedated patients.

Tetanic stimulation is considered a more predictable source of painful stimulus than skin incision and tracheal

intubation.²⁷ However, using a predefined intensity of electric stimulation, that is, 40–60 mA such as is usually delivered during general anesthesia, might expose sedated intensive care unit patients to unnecessary pain and poor tolerance.¹⁴ To overcome this issue, we introduced the pupillary pain index, a new score based on automatically increasing the electric stimulation by stepwise increments of 10 mA until pupil size has increased by $\geq 13\%$ compared to baseline. Considering that pupil reflex dilation changes of $>30\%$ were associated with tachycardia and arterial hypertension,²⁴ a maximal threshold of 13% was arbitrarily chosen to reflect a pupil reaction to noxious stimulation without systemic effects. In other studies, 13%–25% changes in pupil reflex dilation were found significant responses to noxious stimuli.^{16–18} The pertinence of this threshold setting was confirmed in the present study where positive correlation was found between pupillary pain index scores and Behavioral Pain Scale response to endotracheal suctioning during 2 separate measurements (T1 and T2), and no correlation existed between pupillary pain index scores and hemodynamic responses to tetanic stimulation. In a preliminary study, pupillary pain index score was correlated with an observational pain scale in postoperative children.²⁸ In anesthetized patients, pupillary pain index score was significantly reduced where remifentanyl was administered.¹⁹ Collectively, these findings indicate that pupillary pain index score could be viewed as a reliable and consistent measurement of nociception. Individualized titration of opioids in sedated patients could be then possible. Future studies using pupillary pain index as a nonclinic instrument to pilot the administration of analgesics in the intensive care unit are warranted.

Optimizing sedation and analgesia in sedated brain-injured patients is challenging due to the lack of reliable assessments in this population.^{29,30} Detecting pain in sedated brain-injured patients remains difficult and relies on the observation of indirect signs including tachycardia, arterial hypertension, and elevation of ICP during noxious procedures. In this context, we investigated the diagnostic value of pupillary pain index measurements in a group of 20 brain-injured patients meeting criteria to correctly interpret pupil size measurements: (1) a preservation of midbrain function as attested by pupillary light reflex measurements, in line with data from postcardiac arrest patients³¹; and (2) similar pupillary pain index measurements during tetanic stimulation of the ulnar nerve between right and left forearms to rule out a possible impact of focal neurological damage. We indeed found an asymmetric pupillary pain index response according to the location of noxious stimulation in 1 stroke patient with unilateral sensory deficit.³² The similarity of pupil size measurements at baseline and during tetanic stimulation between the 2 groups of patients indicates the preservation of autonomic pathways involved in the transmission of nociception in the group of brain-injured patients. Interestingly, when comparing endotracheal suctioning and tetanic stimulation as noxious stimuli, we found that tetanic stimulation had no or minor impact on ICP. This might be of great interest for the monitoring of nociception in brain-injured patients under sedation to control ICP.

This study has several limitations. First, it was not possible to examine the strength of association between the pupillary pain index score and pain levels in a population of sedated patients unable to self-report their pain for criterion validation. Second, the studied patients are heterogeneous with characteristics that might have affected the variation of Behavioral Pain Scale score. However, it was not feasible to account for these covariables in the construction of the final area under the receiver operating characteristic curve. Third, we chose to combine brain-injured and non-brain-injured patients for 2 main reasons: (1) in this proof of concept study, we aimed at exploring pupil size changes to noxious stimuli in sedated patients providing the absence of focal neurological damage that could have interfered with the interpretation of pupillary pain index measurements; and (2) the construction of 1 global area under the receiver operating characteristic curve for 2 groups of patients assumed an even discriminative performance of pupillary pain index score within the 2 populations. However, we did not have the sample size to confirm this assumption. Evaluating specific properties of pupillary pain index score in each population would require larger population sizes. Fourth, the brain-injured group is heterogeneous with regards to the brain injury. The specific role of the nature, localization, and volume of brain lesions on pupillary pain index scores in these patients is unknown. Fifth, the doses of sufentanil differed between the 2 groups of patients that might have influenced the results. However, no significant difference was found in the pupil reflex dilation measurements between the 2 groups. Nevertheless, the performance of pupillary pain index score during changes of sufentanil dose over time warrants further investigations.

In conclusion, this proof of concept study indicates that nociception could be assessed in sedated critically ill patients, whether they had brain injury or not, through the use of quantitative pupillometry and pupillary pain index score to measure the autonomic reactivity to standardized pain stimulus. In addition, pupillary pain index measurement might be of special interest in the brain-injured population where physiological responses to noxious procedures can increase ICP. ■■

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DISCLOSURES

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