Review

# Evaluating and monitoring analgesia and sedation in the intensive care unit

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## Abstract

Management of analgesia and sedation in the intensive care unit requires evaluation and monitoring of key parameters in order to detect and quantify pain and agitation, and to quantify sedation. The routine use of subjective scales for pain, agitation, and sedation promotes more effective management, including patient-focused titration of medications to specific end-points. The need for frequent measurement reflects the dynamic nature of pain, agitation, and sedation, which change constantly in critically ill patients. Further, close monitoring promotes repeated evaluation of response to therapy, thus helping to avoid over-sedation and to eliminate pain and agitation. Pain assessment tools include self-report (often using a numeric pain scale) for communicative patients and pain scales that incorporate observed behaviors and physiologic measures for noncommunicative patients. Some of these tools have undergone validity testing but more work is needed. Sedation-agitation scales can be used to identify and quantify agitation, and to grade the depth of sedation. Some scales incorporate a step-wise assessment of response to increasingly noxious stimuli and a brief assessment of cognition to define levels of consciousness; these tools can often be quickly performed and easily recalled. Many of the sedation-agitation scales have been extensively tested for inter-rater reliability and validated against a variety of parameters. Objective measurement of indicators of consciousness and brain function, such as with processed electro-encephalography signals, holds considerable promise, but has not achieved widespread implementation. Further clarification of the roles of these tools, particularly within the context of patient safety, is needed, as is further technology development to eliminate artifacts and investigation to demonstrate added value.

## Introduction

Effective management of analgesia and sedation in the intensive care unit (ICU) setting requires an assessment of the needs of the patient, subjective and/or objective measurement of the key variables (such as pain, agitation, and level of consciousness), and titration of therapy to achieve specific targets [1-4]. It is important to recognize that patient needs can differ depending upon clinical circumstances, and that for any given patient therapeutic targets are likely to change over time. Thus, achieving patient comfort and ensuring patient safety, including avoidance of excessive or prolonged sedation, relies on accurately measuring pain, agitation, sedation, and other related variables utilizing validated tools that are easy to use, precise, accurate, and sufficiently robust to include a wide range of behaviors. The consequences of inadequate control of pain or agitation are considerable, but excessive or prolonged sedation is also problematic, leading to increased risk for complications of critical care. In addition to promoting a consistent, goal-directed approach to management, the systematic use of these tools enhances communication among care providers.

Here we review the available subjective instruments for evaluating pain, sedation, and agitation in the critically ill adult patient, as well as the results of validation and clinical application studies. Additionally, although objective tools, such as cerebral function monitoring, have not achieved widespread application in the ICU setting, the principles and potential roles of objective measurements related to analgesia and sedation are discussed.

## Assessment of pain and analgesia

Optimal pain assessment in adult critical care settings is essential because it has been reported that 35% to 55% of

ATICE = Adaptation to Intensive Care Environment; BPS = Behavior Pain Scale; BIS = Bispectral Index; CPOT = Critical Care Pain Observation Tool; CSI = Cerebral State Index; EEG = electroencephalography; EMG = electromyogram; FLACC = Face, Legs, Activity, Cry, Consolability Observational Tool; ICU = intensive care unit; MSAT = Minnesota Sedation Assessment Tool; NPS = Numeric Pain Scale; PSI = Patient State Index; RASS = Richmond Agitation-Sedation Scale; RSS = Ramsay Sedation Scale; SAS = Sedation Agitation Scale; SCCM = Society of Critical Care Medicine; VICS = Vancouver Interactive and Calmness Scale.

nurses underrate the patient's pain [5-7], and in one study [8] 64% of patients did not receive any medications before or during painful procedures. In the SUPPORT (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment) study [9], nearly 50% of patients reported pain, 15% reported moderately or extremely severe pain that occurred at least half of the time, and nearly 15% were dissatisfied with their pain control. Inaccurate pain assessment and the resulting inadequate treatment of pain in critically ill adults can have significant physiologic conse-quences. For example, pain increases myocardial workload, which can lead to myocardial ischemia, or to splinting, atelectasis, and a cascade of events that in turn can lead to pneumonia [10].

Patient self-report is the best indicator of pain, specifically using the numeric pain rating scale ranging from 0 to 10. However, many critically ill patients are unable to communi-cate effectively because of cognitive impairment, sedation, paralysis, or mechanical ventilation. Identification of the optimal pain scale in such patients is ongoing, and no single tool is universally accepted for use in the noncommunicative patient [1,11]. When a patient cannot express themself, observable indicators - both physiologic and behavioral - have been treated as pain-related behaviors to evaluate pain in this population [12,13]. National pain guidelines support evalua-tion of both physiologic and behavioral response to pain in patients who are unable to communicate [14]. Additionally, in the Clinical Practice Guidelines for Sustained Use of Sedatives and Analgesics in the Critically Ill Adult published by the Society of Critical Care Medicine (SCCM) [1], regular assessment and documentation of pain and response to therapy is recommended (grade C).

There is a direct relationship between the ability to assess and document a patient's pain and the ability to manage pain [15,16]. However, Gelinas and coworkers [17] found that of 183 documented pain episodes in intubated patients, use of a pain scale was mentioned in only 1.6% of cases. Although assessment of patient pain behaviors was common (73% of episodes), these assessments were observed and documented without the use of a valid and reliable pain tool. In a recent description of 1,360 mechanically ventilated, critically ill patients, Payen and coworkers [18] found that pain was not assessed in 53% of patients who were receiving analgesia, and when pain was assessed specific pain tools were used only 28% of the time. Inadequate pain control is largely due to inconsistent use of standardized tools. Therefore, use of a valid and reliable tool to assist health care providers in the management of pain in the critically ill, sedated patient is paramount [1,19].

## Pain assessment: communicative patients
The Numeric Pain Scale (NPS) employs a verbal rating of pain on a scale from 0 to 10, with 10 being the worst pain ever experienced, and is broadly used in a variety of clinical

settings. It has been successfully used to evaluate pain in older adults [20], change in pain intensity [21], assessment of pain reduction [22], and evaluation of pain in geriatric patients [23], as well as in communicative critically ill patients to evaluate procedural pain [24]. Self-reported pain is considered to be the standard, and the NPS is recommended by SCCM (grade B recommendation). However, data to support its efficacy compared with other pain tools used in the noncommunicative patient are limited.

## Pain assessment: noncommunicative patients
A variety of tools focusing on behavioral and physiologic indicators of pain are being used to evaluate pain intensity in noncommunicative patients, but evidence of their validity and reliability in critically ill patients is limited. Two pain scales presently used in adult critical care settings (COMFORT scale and the Face, Legs, Activity, Cry, Consolability Observational Tool [FLACC] scale) were originally developed and validated in the pediatric population. Although noncommunicative critically ill adults are similar to newborns, infants, and preverbal toddlers in being unable to report and describe pain, some behavioral components of these tools for children are not applicable to adults. Furthermore, validation of these tools in adults is limited.

### Pediatric pain tools adapted for use in adults
The COMFORT scale contains behavioral and physiologic factors (eight items, each scored from 1 to 5) to evaluate pain and was originally designed to assess distress in pediatric ICU patients [25]. The scale measures alertness, calmness, facial tension, physical movement, muscle tone, ventilator respiratory response, blood pressure and heart rate, and it exhibits good inter-rater reliability [26].

The FLACC was developed to provide a simple and consis-tent method for nurses to identify, document, and evaluate pain in children [27,28]. The FLACC scale assesses pain by using behavioral indicators and assessment of body move-ments (face, legs, activity), verbal responses (cry), and consolability. It has been validated for assessing pain in children with cognitive impairment, in young children [29] and in children with postoperative pain [27], and in comparison with children's self report of pain [30]. However, there are few data to support its use in adult critically ill patients. Specific components such as cry and consolability are not appropriate for the critically ill, intubated adult.

### Adult-specific pain tools
The Behavior Pain Scale (BPS) [15] is based on a sum score of three items: facial expression, movements of upper limbs, and compliance with mechanical ventilation. Based upon the assumption that a relationship exists between each score and pain intensity, each pain indicator is scored from 1 (no response) to 4 (full response), with a maximum score of 12. Initial validity and reliability was established using 269 assessments in 30 sedated mechanically ventilated patients

during painful procedures (endotracheal suctioning and mobilization) as well as nonpainful procedures (compression stocking application, central venous catheter dressing change). Nociceptive stimulation resulted in higher BPS values than did non-nociceptive stimuli (4.9 versus 3.5; $P < 0.01$), whereas the groups had comparable scores prior to stimulation. Excellent inter-rater reliability was also found during multiple testing ($r^2 = 0.50$ to 0.71). Young and co-workers [30] conducted additional validity and reliability testing of the BPS in critically ill patients during routine painful and nonpainful procedures. A significant ($P < 0.003$) increase in BPS scores was found after painful procedures, and no significant increase was found after the nonpainful procedure. The odds of an increase in BPS between pre-procedure and post-procedure assessments were more than 25 times higher for repositioning (painful) compared with eye care (nonpainful; $P < 0.0001$), after controlling for analgesics and sedatives. A limitation of BPS is that responsiveness (increase in score in response to noxious stimuli) decreases substantially with deepening levels of sedation [15]. In addition, because compliance with mechanical ventilation may be considered to be a separate domain from the other behaviors, some intensivists only score facial expression and movements of upper limbs in order to assess the individual pain state.

Chanques and coworkers [31] evaluated pain in 230 ICU patients using the combination of BPS (for noncommunicative patients) and NPS (for communicative patients). The periods considered were a 21-week control phase with usual care as regards pain evaluation, and a subsequent 29-week intervention phase, during which nurses assessed pain levels using the two tools and notified physicians of high pain levels. The incidence of pain as well as the rate of severe pain events decreased significantly during the intervention phase. A significant decrease in the duration of mechanical ventilation was also noted [18].

The Adult Nonverbal Pain Scale is a modification of the FLACC scale and was developed for use in adult, non-communicative patients. It evaluates five parameters: face, activity, guarding, physiologic I (vital signs), and physiologic II (skin and pupils). It has been pilot tested in a burn-trauma unit during all three patient care shifts in 200 paired assessments with the FLACC scale [32]. It exhibited good correlation with the FLACC scale ($r = 0.86$, $P < 0.001$). Although it shows promise as a tool for use in the nonverbal adult population, it has not been evaluated against any other measures of pain in the adult population.

A recently developed behavior pain tool, the Critical Care Pain Observation Tool (CPOT), has four components: facial expression, body movements, muscle tension, and compliance with the ventilator for intubated patients or vocalization for extubated patients. Each of these behaviors is assigned a rating of 0 to 2. The CPOT was adapted from

three different pain assessment tools [15,25,33] and three different descriptive/qualitative studies [13,17,34]. Gelinas and coworkers [34] conducted a validation study in 105 cardiac surgery patients, using periods of rest, nociception, and 20 minutes after the nociceptive procedure (positioning) during three separate testing periods while patients were conscious and unconscious. The tool exhibited criterion validity because significant associations were found between the patients' self-reports of pain and CPOT, whereas discriminant validity was supported by higher scores during the nociceptive procedure compared with the score at rest. Inter-rater reliability was also good. Of note, changes in scores with nociceptive stimulation were similar whether the patient was conscious or unconscious.

Current practice for adult ICU patients commonly includes a combination of NPS or similar self-reported pain quantification tool, plus an instrument designed to identify pain using behavior and physiologic parameters in the noncommunicative patient. This sequential approach is supported in the form of grade B recommendations from the SCCM [1]. More work is needed to provide convincing evidence of the validity of these tools as well as to address limitations in application, such as how to assess for pain in the presence of heavy sedation. Although new scales and additional validation studies are frequently reported in this evolving field, we support use of either the BPS or CPOT for noncommunicative scales (Tables 1 and 2). Combining pain testing with a standardized approach to management can lead to better pain control without prolonging the duration of mechanical ventilation [31].

## Sedation and agitation scales

The Ramsay Sedation Scale (RSS) was introduced more than 30 years ago as a subjective tool with which to evaluate precisely the level of consciousness during titration of sedative medications in the ICU [35]. Since then, numerous subjective instruments have been developed, validated, and applied in clinical and research settings to monitor level of consciousness or arousal, as well as to evaluate cognition, agitation, patient-ventilator synchrony, and other parameters. These include the Sedation Agitation Scale (SAS) [36], the Motor Activity Assessment Scale [37], the Vancouver Interactive and Calmness Scale (VICS) [38], the Richmond Agitation-Sedation Scale (RASS) [39], the Adaptation to Intensive Care Environment (ATICE) instrument [40], and the Minnesota Sedation Assessment Tool (MSAT) [41] (Table 3). In order for such a tool to be effective in the busy ICU setting, the users must be confident that it accurately measures what is intended, that it is reliable, and that it is easy to apply repeatedly by multiple care providers [42]. Desirable features of a good sedation scale have been enumerated and include the following [43]: rigorous multidisciplinary development; ease of administration, recall, and interpretation; well defined discrete criteria for each level; sufficient sedation levels for effective drug titration; assessment of agitation; and

**Table 1**

**Behavioral Pain Scale**

| Item | Description | Score |
|---|---|---|
| Facial expression | Relaxed | 1 |
| | Partially tightened (for example, brow lowering) | 2 |
| | Fully tightened (for example, eyelid closing) | 3 |
| | Grimacing | 4 |
| Upper limbs | No movement | 1 |
| | Partially bent | 2 |
| | Fully bent with finger flexion | 3 |
| | Permanently retracted | 4 |
| Compliance with ventilation | Tolerating movement | 1 |
| | Coughing but tolerating ventilation for most of the time | 2 |
| | Fighting ventilator | 3 |
| | Unable to control ventilation | 4 |

Scores from each of the three domains are summed, with a total score of 3 to 12 [15].

**Table 2**

**Critical Care Pain Observational Tool**

| Indicator | Description | Score |
|---|---|---|
| Facial expression | No muscular tension observed | Relaxed, neutral: 0 |
| | Presence of frowning, brow lowering, orbit tightening, and levator contraction | Tense: 1 |
| | All of the above facial movements plus eyelid tightly closed | Grimacing: 2 |
| Body movements | Does not move at all (does not necessarily mean absence of pain) | Absence of movements: 0 |
| | Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements | Protection: 1 |
| | Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed | Restlessness: 2 |
| Muscle tension | No resistance to passive movements | Relaxed: 0 |
| | Resistance to passive movements | Tense, rigid: 1 |
| | Strong resistance to passive movements, inability to complete them | Very tense or rigid: 2 |
| Compliance with the ventilator | Alarms not activated, easy ventilation | Tolerating ventilator or movement: 0 |
| | Alarms stop spontaneously | Coughing but tolerating : 1 |
| | Asynchrony: blocking ventilation, alarms frequently activated | Fighting ventilator: 2 |
| OR | | |
| Vocalization (extubated patients) | Talking in normal tone or no sound | Talking in normal tone or no sound: 0 |
| | Sighing, moaning | Sighing, moaning: 1 |
| | Crying out, sobbing | Crying out, sobbing: 2 |

Scores for each of the four domains are summed, with a total score of 0 to 8 [34].

demonstration of inter-rater reliability and evidence for validity in relevant patient populations.

## Recommendations and use of sedation scales in intensive care units

The routine use of a sedation scale in ICU patients who are receiving sedative medications is endorsed in SCCM's Clinical Practice Guidelines for Sustained Use of Sedatives and Analgesics in the Critically Ill Adult [1] and is supported by other expert reviews [2-4]. The SCCM guidelines specifically recommend that a sedation goal or end-point should be established and regularly redefined for each patient, and that regular assessment and response to therapy should be systematically documented (grade C recommendation) [1]. The use of a validated sedation assessment scale was also specifically recommended (grade B recommendation). Additionally, the treatment algorithm depicted in the guidelines indicate that clinicians should use a sedation scale

**Table 3**

**Sedation and sedation-agitation scales**

| Scale (year developed) [ref.] | Scale design | Reliability | Validity |
|---|---|---|---|
| Ramsay Sedation Scale (RSS; 1974) [35] | Six levels: four levels of sedation defined by responses to stimuli (levels 3 to 6), a level of 'cooperative, oriented, and tranquil' (level 2), and a level for 'anxious, agitated, or restless' (level 1) | $K = 0.94$, RNs [58] | Versus RASS ($r = -0.78$) [39]; Versus BIS ($P < 0.01$) [63]; Versus BIS v2.10 ($r = -0.27$) [64]; Versus BIS XP v3.10 ($r = -0.40$) [64] |
| Sedation Agitation Scale (SAS; 1994) [85] | Seven levels: three levels of agitation (levels 5 to 7), a 'calm and cooperative' level (level 4), and three levels of sedation (levels 1 to 3). All levels are defined by multiple (3 or 4) criteria | $r^2 = 0.83$, $K = 0.92$ [36]; $K = 0.93$ [59]; $K = 0.85$ investigators [59]; $K = 0.87$ RNs [59] | Versus RSS ($r^2 = 0.83$) [36]; Versus VAS sedation $r = -0.77$) [59]; Versus Harris ($r^2 = 0.86$) [36]; Versus BIS ($r^2 = 0.21$) [65]; Versus VAS, researcher ($r = 0.9$) [61]; Versus VAS, nurses ($r = 0.43$) [61]; Versus BIS 3.2 ($r = 0.6$) [61]; Versus BIS ($r = 0.36$) [66]; Versus BIS, exclude motor excess ($r = 0.50$) [66]; Versus BIS ($r^2 = 0.48$ before, 0.44 after stimulation) [67]; Versus digital imaging [70]; Versus BIS XP ($r = 0.725$) [68]; Versus BIS v2.1.1 ($r = 0.376$) [68] |
| Motor Activity Assessment Scale (MAAS; 1999) [37] | Seven levels: three levels of agitation (levels 4 to 6), a 'calm and cooperative' level (level 3), and three levels of sedation (levels 0 to 2). All levels are defined by multiple (3 to 4) criteria | $K = 0.83$ (95% CI 0.72 to 0.94) [37]; $r = 0.81$, 3RN, 1MD, 1PharmD [60] | Versus VAS ($P = 0.001$) [37]; Versus BP ($P = 0.001$) [37]; Versus HR ($P = 0.001$) [37]; Versus agitation-related sequelae ($P = 0.001$) [37] |
| Vancouver Interactive and Calmness Scale (2000) [38] | Contains two domains ('interaction' and 'calmness'). Each domain has five questions, and each question has six responses from 'strongly agree' to 'strongly disagree'. Patient stimulation required for some questions. Scores are summed (maximum 30/domain), with higher scores for calm and interactive | $r = 0.89$ for calmness score; $r = 0.90$ for interactive score | Calmness score versus need for intervention $r = -0.83$ [38]; Minimal clinical important difference, calmness = -2.2 [38]; Minimal clinical important difference, interaction = 2.5 [38]; Guyatt's responsiveness statistic, calmness = -1.4 [38]; Guyatt's responsiveness statistic, interaction = 2.3 [38] |
| Richmond Agitation-Sedation Scale (RASS; 2002) [39] | Ten level scale: four levels of agitation (levels +1 to +4), a level for 'calm and alert' (level 0), and five levels of sedation (-1 to -5) defined by response to verbal then physical stimulation, plus consideration of cognition and sustainability | $r = 0.956$, $K = 0.73$ for five raters (2 MD, 2 RN, and 1 PharmD) [39]; $r = 0.964$, $K = 0.80$ nurse educator versus 27 RNs [39]; $K = 0.91$ RN [58]; $K = 0.89$ RN versus rater [90]; $K = 0.77$ RN versus rater [90] | Versus VAS $r = 0.93$ (95% CI 0.84 to 0.98) [39]; Versus GCS ($r = 0.79$) [39]; Versus RSS ($r = -0.78$) [39]; Versus SAS ($r = 0.78$) [39]; Differences in consciousness ($P < 0.001$) [58]; Fluctuation in consciousness ($P < 0.001$) [58]; Versus attention screening ($r = 0.78$) [58]; Versus GCS ($r = 0.91$) [58]; Versus quantity of Rx ($r = -0.31$) [58]; Versus BIS ($r = 0.63$) [58]; Face validity 92% agreed [58]; Versus BIS XP ($r = 0.81$) [68]; Versus BIS v2.1.1 ($r = 0.30$) [68]; Versus BIS XP ($r^2 = 0.36$) [69]; Versus BIS 3.4 ($r^2 = 0.20$) [69]; Versus actigraphy ($r = 0.58$) [62]; Versus COMFORT scale ($r = 0.75$) [62] |

*Continued overleaf*

**Table 3 (continued)**

| Scale (year developed) [ref.] | Scale design | Reliability | Validity |
|---|---|---|---|
| Adaptation to Intensive Care Environment (ATICE; 2003) [40] | Five tests in two domains: consciousness and tolerance domains. Tests included in the consciousness domain: awakeness scale (five levels from 0 = eyes closed, no mimic, to 5 = eyes open spontaneously, based on verbal then physical stimulation) and comprehension scale (score based on summing 1 point each for positive response to five commands). Tests included in the tolerance domain: calmness scale (four levels from 3 = calm to 0 = life-threatening agitation), ventilator synchrony scale (score based on summing 1 point for each of four observed events) and face relaxation scale (four levels from 3 = relaxed face to 0 = permanent grimacing) | $r$ = 0.86 to 0.99 RN versus MD [40] $r$ = 0.82 to 0.99 RN versus research RN [40] $r$ = 0.91 to 0.99 research RN versus MD [40] | Internal consistency = 0.67 to 0.87 [40] Versus RSS ($r$ = 0.40 to 0.86) [40] Versus SAS ($r$ = 0.37 to 0.75) [40] Versus GCS ($r$ = 0.78 to 0.95) [40] Versus COMFORT scale ($r$ = 0.38 to 0.83) [40] Versus VAS ($r$ = 0.41 to 0.92) [40] Versus sedative plus analgesics ($r$ = 0.45 to 0.72) [40] |
| Minnesota Sedation Assessment Tool (MSAT; 2004) [41] | Two domains: arousal and motor activity. Arousal is a six-level scale (1 = deeply sedated to 6 = alert) based on eye opening or movement responses to verbal then physical stimulation. Motor scale has four levels (1 = no movement to 4 = central muscle group movement) | Arousal scale K = 0.85 [41] Motor scale K = 0.72 [41] | Arousal scale: $r$ = 0.68 versus VICS [41] Motor scale: $r$ = -0.41 versus calmness subscale of VICS [41] Convergent validity present for arousal and motor [41] Predictive validity present for arousal only [41] |

BIS, Bispectral Index; CI, confidence interval; GCS, Glasgow Coma Scale; K, κ statistic; MD, physician; PharmD, pharmacist; RN, registered nurses; VAS, visual-analog scale.

to assess for agitation/anxiety [1]. Historically, the use of a sedation scale has been disappointingly low, with sedation assessment performed in fewer than one-half of ICU patients, ICUs, and days of observation in multiple studies from throughout the world [44-50].

Although all of the aforementioned studies were performed before publication of the SCCM guidelines in 2002, a recently reported prospective surveillance study conducted in 44 ICUs during 2004 revealed that sedation assessment is still not performed in many patients who are receiving sedative drugs [18]. For example, on the second ICU day, 72% of patients were receiving sedative medications but only 43% received sedation assessment. The missed opportunity to titrate medications effectively by using a sedation scale is apparent, because 57% of assessed patients were under deep sedation [18].

### Structure of sedation scales

Each sedation scale is constructed somewhat differently (Table 3), although there are several common themes regarding domains to be evaluated and the structure of the instrument. The key domain of most scales is consciousness, typically ranging from alert to comatose, with a subdomain of arousal or awakeness, often in response to stimuli of increasing intensity (as with RSS, RASS, ATICE, and MSAT). In addition, higher states of consciousness may be further defined by testing cognition or comprehension (as with RASS and ATICE), or sustainability (as with RASS). These instruments (RSS, RASS, ATICE, and MSAT) rely upon noting a simple response (movement, eye opening, or following a command such as 'look at me') spontaneously or responses to simple cues (speaking to the patient or physically stimulating the patient) that proceed in a logical progression reflecting progressively deeper sedation [42]. This structure produces little overlap in levels of consciousness because of the step-wise approach, but the assessment can be quickly performed and the results easily recalled. In contrast, the structure of some instruments is to sum multiple subscales [38,40] or to test multiple criteria for each sedation level [36,37], thus adding complexity and potentially impairing ease of recall.

### Assessment of agitation

Assessment of agitation, or conversely of calmness, is another important domain that is measured using many sedation instruments, either as a distinct subscale (VICS and ATICE) or incorporated into a single scale (SAS, MAAS, and RASS). With RASS various levels of agitation are assigned positive numbers, whereas sedation levels receive negative numbers, providing distinction despite the single scale design. Research suggests that the majority of ICU patients exhibit agitation at some time during their ICU stay [51]. This is an important patient safety concern because behaviors such as aggressive behavior against care givers or self-removal of an important tube or catheter can have serious

consequences [52-55]. Use of a sedation-agitation scale can enhance identification of agitation or anxiety, thus prompting therapeutic intervention [1] and reducing the subsequent incidence of agitation [31], as well as leading to identification and better management of pain, delirium, or other conditions that might produce agitation [2,51,54, 56,57]. It is worth emphasizing that agitated behavior may be a manifestation of inadequate pain control or it could be due to distress from a problem that requires immediate attention, such as a malpositioned endotracheal tube or myocardial ischemia.

### Testing of validity and reliability

ICU sedation instruments that have been tested for inter-rater reliability and validity in multiple patient populations are summarized in Table 3, listed in order of year of publication. Inter-rater reliability has been formally tested in research investigators, as well as in clinical ICU nurses, for most of these instruments, as noted in Table 3 [36-41,58-60]. It is noteworthy that some scales such as SAS and RASS have been tested extensively, including as many as five raters representing nurses, physicians, and pharmacists, in research and clinical settings, at multiple hospitals, and in different patient populations (with or without mechanical ventilation). Excellent reliability has been demonstrated for the majority of scales. Face, construct, or criterion validity has been demonstrated for many of the domains of these instruments using a variety of comparators. These comparators include expert opinion [40,41,59], quantity of sedative drug administered [40,41,58], visual-analog scales [39,59,61], other sedation instruments [36,39,41,58,62], processed electroencephalography (EEG) such as Bispectral Index (BIS) and Patient State Index (PSI) [61,63-69], and limb acceleration and movement using actigraphy [62] or digital imaging [70] (Table 3). In most cases good to excellent validity is demonstrated. Far less work has been conducted to validate the agitation domain of sedation-agitation scales. Additionally, some scales incorporate domains that are more difficult to validate. For example, the motor activity domain of the MSAT exhibited only weak correlations with the comparator (the VICS calmness scale).

### Impact of the use of sedation scales

Implementation of a sedation assessment instrument can have a positive impact on precision of sedative administration [71,72], with greater frequency of appropriate sedation level and lower incidence of over-sedation, reduction in sedative and analgesic drug doses, shorter duration of mechanical ventilation, and even reduced use of vasopressor medications. Implementation of strategies that incorporate scheduled assessment for agitation, within the context of additional monitoring and targeted management, has been associated with a reduction in agitation, shorter duration of mechanical ventilation, and even fewer nosocomial infections [31,57]. Use of a sedation scale is an integral component of most patient-focused management algorithms.

The regular performance and documentation of level of sedation and agitation using a logical, easy to use, validated instrument is strongly recommended because it promotes optimal patient-focused sedation management. The authors endorse RSS and RASS (Tables 4 and 5, respectively) as sedation scales, which have excellent inter-rater reliability and validity, and were the most frequently used sedation scales in the latest survey [18].

## Objective measurement of cerebral function in the intensive care unit setting

The intense management of the conscious state and mental well being are as important as critical care for any other major organ system. The brain is the most important organ in the human body, but it is not closely monitored routinely in most ICUs. Sedation scoring systems have been well validated for the management of sedation in the critical care environment, with improved outcomes when they are used effectively. Cerebral function monitors offer a more objective method of monitoring both sedation level and mental well being in the ICU. The electrical activity recorded from the cortex of the brain may be affected by cerebral perfusion, cerebral metabolism, hypoxia, sedative pharmacologic agents, and seizure activity. Cerebral insults may be detected early while they are still reversible, so that therapeutic measures may be taken. Therefore, as part of the patient safety culture now being developed in the health care system, cerebral function monitoring may be a vital tool in pursuing this objective.

### Cerebral function monitors

The available cortical activity monitors record the cortical EEG signals and use the frequency, power, or disorder of these signals to determine the patient's status. These monitors process data through various proprietary algorithms to a dimensionless number that reflects the depth of sedation of the brain. The effect of sedative drugs on the electrical activity of the human brain was first reported in 1937 [73]. The very sensitive 20-channel devices were not conducive to routine clinical monitoring, so in 1969 a simpler two-channel device was developed that recorded cortical activity as a continuous power strip. The width of the power band was dependent on the amount and frequency of the cortical electrical signal [74]. Since then many different methodologies have been developed to process and simplify the EEG signal. The overall goal was to quantify the EEG signal in a display that can be easily interpreted by the practitioner. The Cooley and Tukey algorithm applied to the Fourier theorem - the Fast Fourier Transform - allows a power versus frequency histogram to be developed that may be displayed as a spectral array. This concept has led to application of these monitors as tools for the objective measurement of the depth of sedation. However, this approach relies on the concept that consciousness lies at a cortical level, which perhaps is an over-simplification of a very complex process. Cortical electrical activity may only be an expression of consciousness.

**Table 4**

**Ramsay Sedation Scale**

| Score | Definition |
|---|---|
| 1 | Anxious and agitated or restless or both |
| 2 | Cooperative, oriented, and tranquil |
| 3 | Responds to commands only |
| 4 | Brisk response to a light glabellar tap or loud auditory stimulus |
| 5 | Sluggish response to a light glabellar tap or loud auditory stimulus |
| 6 | No response to a light glabellar tap or loud auditory stimulus |

Performed using a series of steps: observation of behavior (score 1 or 2), followed (if necessary) by assessment of response to voice (score 3), followed (if necessary) by assessment of response to loud auditory stimulus or light glabellar tap (score 4 to 6) [35].

**Table 5**

**Richmond Agitation-Sedation Scale**

| Score | Term | Description |
|---|---|---|
| +4 | Combative | Overtly combative or violent, immediate danger to staff |
| +3 | Very agitated | Pulls on or removes tube(s) or catheter(s) or exhibits aggressive behavior toward staff |
| +2 | Agitated | Frequent nonpurposeful movement or patient-ventilator dys-synchrony |
| +1 | Restless | Anxious or apprehensive but movements not aggressive or vigorous |
| 0 | Alert and calm | |
| -1 | Drowsy | Not fully alert, but has sustained (>10 seconds) awakening, with eye contact, to voice |
| -2 | Light sedation | Briefly (<10 seconds) awakens with eye contact to voice |
| -3 | Moderate sedation | Any movement (but no eye contact) to voice |
| -4 | Deep sedation | No response to voice, but any movement to physical stimulation |
| -5 | Unarousable | No response to voice or physical stimulation |

Performed using a series of steps: observation of behaviors (score +4 to 0), followed (if necessary) by assessment of response to voice (score -1 to -3), followed (if necessary) by assessment of response to physical stimulation such as shaking shoulder and then rubbing sternum if no response to shaking shoulder (score -4 to -5) [39].

The BIS (Aspect Medical Systems, Norwood, MA, USA) is composed of time domain, frequency domain, and high-order spectral subparameters. This integrates several disparate descriptors using a proprietary algorithm into a dimensionless index. The BIS algorithm has been compared with a growing database of clinical data and continues to be updated. The resulting BIS number has been correlated with a minimal value that should be attained to prevent patient awareness under anesthesia or sedation [75]. The BIS displays a raw EEG trace obtained from a two-channel sensor but only from a unilateral prefrontal lobe site, and a power trend is displayed with a number from 0 to 100 (0 indicating no cortical activity and 100 a patient who is wide awake). There are no units of measurement and one patient's response to a sedation agent may be dependent on many factors, so whether a BIS number can correlate uniformly with depth of sedation remains controversial. The effect of the electromyogram (EMG) signal may artificially increase the BIS number. This can be detected by viewing the raw signal and seeing the high frequency of the EMG signal within the low voltage signal from EEG. Filters designed to remove the EMG signal have limited efficiency with any of the cortical monitors. However, the EMG signal may be used as a guide to the elimination of muscle relaxant drugs and the return of muscle activity - another type of twitch monitor.

The PSI, displayed on the Sedline Monitor (Hospira, Lake Forest, IL, USA), is another approach to quantifying cerebral cortical activity. This monitor has four channels and monitors both hemispheres of the brain. Similar to the BIS, the PSI converts the raw EEG signal using the Fast Fourier Theorem and a proprietary algorithm to display a dimensionless scale from 0 to 100 that reflects the depth of sedation of the patient. The scale is updated every 1.2 seconds, which makes this monitor quick to respond to changes in cerebral cortical activity. The PSI algorithm was constructed following an analysis of the quantitative EEG changes that accompanied the loss and return of consciousness after administration of sedative drugs. It was validated in a large database of patients and volunteers [76].

The Cerebral State Monitor (Danmeter A/S, Odense, Denmark) is a handheld wireless device that also uses a proprietary algorithm and a 0 to 100 scale, with 40 to 60 indicating an adequate depth of hypnosis. The Cerebral State Index (CSI) that is calculated by the device is derived from the time and frequency domain analysis, which inputs into a fuzzy logic inference system that calculates the index. In a comparative study, both the BIS and the CSI had a predictive probability statistic for depth of anesthesia of 0.87, which demonstrates good performance [77]. The CSI performed better for deeper levels of anesthesia than the BIS, which was better at lighter levels.

The Narcotrend monitor (MonitorTechnik, Bad Bramstedt, Germany) is another monitor that processes raw EEG signals using one-channel or two-channel recordings from different electrode positions. Early models graded the depth of hypnosis into five stages from A (awake) to F (very deep level of anesthesia). The latest Narcotrend software (version 4.0)

**Figure 1**
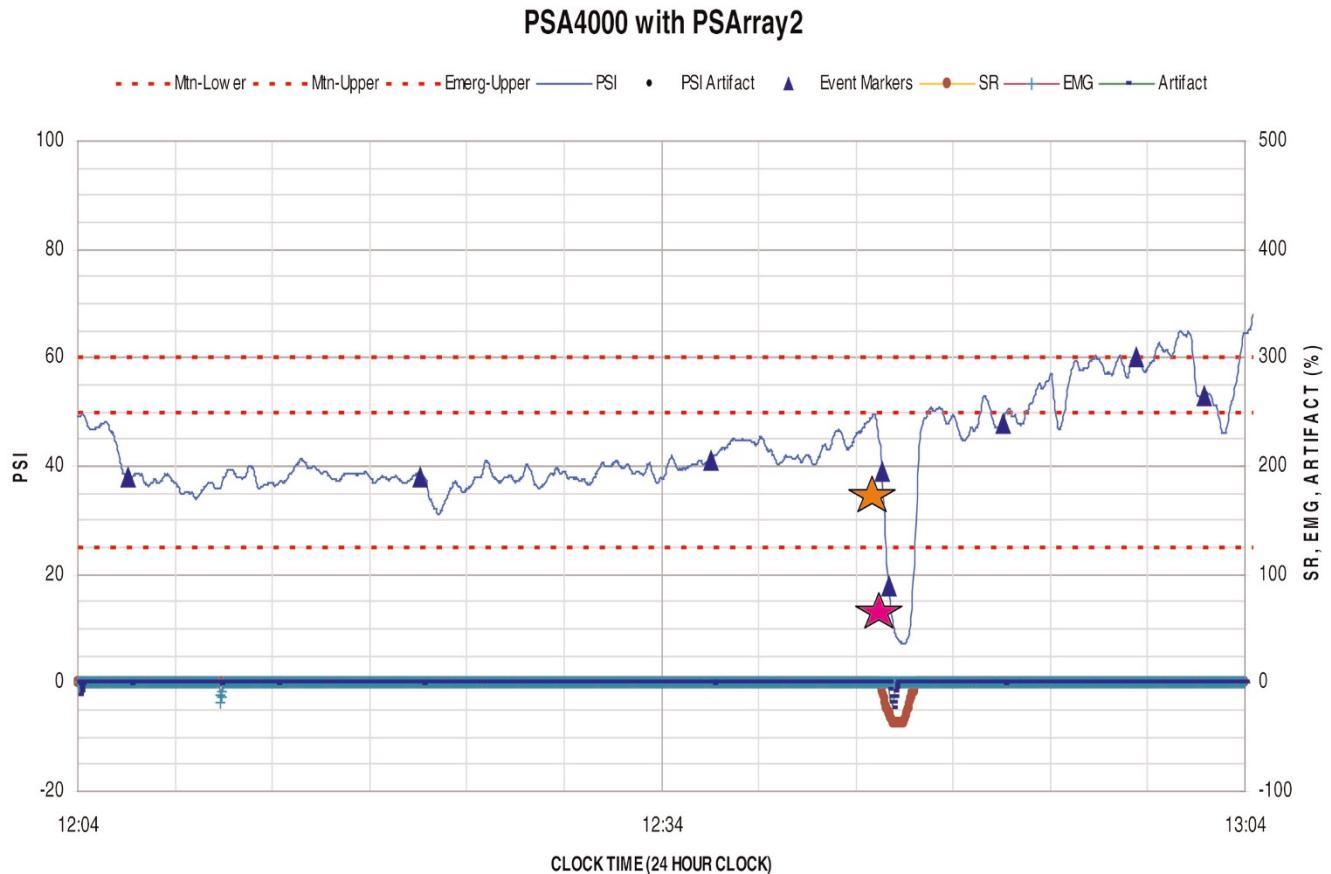


The jagged blue line represents display of Patient State Index (PSI) and suppression ratio (SR) is shown by the red line falling below 0, over time. Solid triangles represent stimulation of patient and stars represent onset and offset of ventricular tachycardia (VT). Ventricular tachycardia with hypotension resulted in a precipitous fall in PSI and SR, with recovery following termination of VT. Reproduced with permission from Ramsay M: Role of brain function monitoring in the critical care and perioperative settings. *Semin Anesth Periop Med Pain* 2005, 24:195-202. [89].

now calculates the Narcotrend Index, another dimensionless 0 to 100 scale that is similar to those calculated by the monitors described above. When compared with BIS, the performance of the Narcotrend Index in terms of prediction probability of depth of sedation was slightly better than BIS (predictive probability statistic 0.88, as compared with 0.85) [78].

**Additional approaches to brain monitoring**
Additional approaches to brain monitoring in the ICU include response entropy and state entropy [79]. The irregularity of the EEG signal can be quantified, and by using an algorithm that is in the public domain, quantified to reflect depth of sedation. This Entropy Monitor (GE Healthcare, Fairfield, CT, USA) utilizes the EMG signal, which may provide information useful for assessing whether a patient is responding to an external stimulus, for instance a painful stimulus. The combination of EEG and EMG is presented as the response entropy, and the lower frequency EEG signals alone are presented as the state entropy. The prediction probability

values of the entropy indices for differentiating between consciousness and unconsciousness are high and comparable with those for BIS [80]. Noxious stimulation does increase the difference between response entropy and state entropy, but an increase in the difference does not always indicate inadequate analgesia [81].

Auditory evoked responses have extensively been studied with increasing depths of sedation [82]. Auditory stimuli stimulate the auditory axis, and the middle-latency auditory evoked responses are reduced in amplitude and elevated in terms of latency with increases in sedation. This Auditory Evoked Potential monitor (Danmeter A/S) studies more than just cortical electrical activity. The monitor uses an algorithm that calculates a numerical index, the Alaris Auditory Response Index (AAI™), from the latency and amplitude of the evoked potential. AAI™ transforms the AEP (auditory evoked potential) and the EEG signal into a value on a 0 to 100 scale that is used to measure depth of sedation. This index correlates well with the BIS index [83].

**Figure 2**
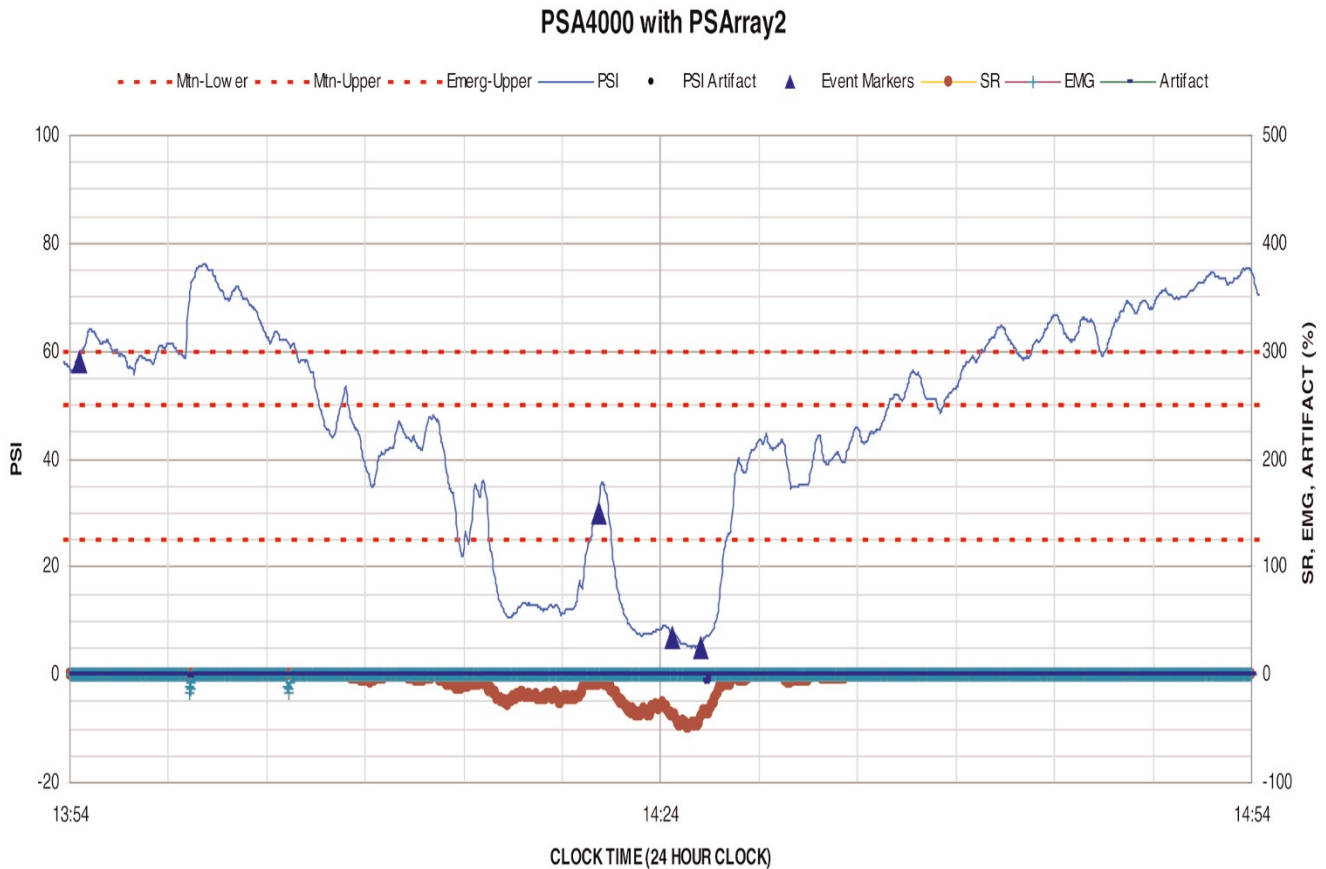


The jagged blue line represents display of Patient State Index (PSI) and suppression ratio (SR) is shown by the red line falling below 0, over time. Solid triangles represent stimulation of patient.  Accidental mis-programming of propofol infusion rate resulted in a steady decline in PSI and SR over time. Recognition of mis-programmed rate was recognized and corrected, resulting in return of PSI and SR to baseline values. Reproduced with permission from Ramsay M: Role of brain function monitoring in the critical care and perioperative settings. *Semin Anesth Periop Med Pain* 2005, 24:195-202. [89].

## The current role of objective cerebral function monitoring in the intensive care unit

The use of these cerebral function monitors as objective monitors of depth of sedation in the ICU has not yet been universally embraced. This is because many factors may alter the signal in the critically ill patient, particularly EMG signals, which can cause erroneously high BIS and PSI scores. These artifacts can be identified by observing the raw EEG signal and seeing a very high frequency low voltage 'noise' within the EEG signal. Thus, an understanding of the basic EEG signal is important to interpreting the data presented by these cerebral function monitors. A variety of confounders, including EMG interference, sleep, drugs such as catecholamines, and temperature changes, may influence the BIS value [84]. In a comprehensive review, LeBlanc and colleagues [84] demonstrated mixed results when BIS was correlated with clinical sedation scales, with $r^2$ ranging from 0.21 to 0.93. Much of the variability is probably related to EMG interference, because BIS values decline significantly when muscle relaxants are administered to ICU patients [85,86].

Where does cerebral function monitoring fit into current ICU practice? The recommendations found in SCCM's Clinical Practice Guidelines, published in 2002, do not endorse routine use [1]. They state that 'objective measures of sedation such as BIS have not yet been evaluated and are not yet proven in the ICU', based upon grade C evidence. Although there is evidence for better operating room outcomes, such as early recognition of unintended awareness [75] or better anesthetic management [87], such evidence is scant in the ICU setting. The incidence of unintended awareness in the ICU is unknown and is mainly observed in those patients who are paralyzed either as a result of their disease process or the use of muscle relaxants. This patient group may be well served by monitoring, because the sequelae of inadequate sedation are severe. Accordingly, use of cerebral function monitoring is likely to be of greatest benefit in patients who

are deeply sedated or who are receiving muscle relaxant medications [1,88]. The most compelling reason to promote further research and clinical experience in cerebral function monitoring in the ICU is patient safety. Examples of changes in PSI in response to clinical events are noted in Figures 1 and 2 [89]. Cerebral insults may be detected at a stage when they are still reversible. The brain is the most complex and most important organ in the human body and deserves more attention than it currently receives. Cerebral function monitors may provide another level of safety for our patients and, as this area of technology advances, improved care of the mental and cognitive functions of the critical care patient is likely to follow.

## Conclusion

Evaluation and monitoring of pain, agitation, and level of consciousness can be accomplished by subjective scales that can contribute to enhanced communication among care givers and to more effective analgesia and sedation management. These relatively simple tools can be repeatedly applied, promoting close monitoring of changing circumstances and response to therapy. Some instruments add other measures of patient tolerance of the ICU environment, such as patient-ventilator synchrony. More work is needed to promote more widespread use of these tools and to address barriers to implementation. Furthermore, strategies that examine multiple aspects of patient distress and comfort, including tolerance to the ICU and interventions, are increasingly important. Future directions also include advancing the technology of objective monitoring of cerebral function in order to allow better adaptation to the ICU setting (as compared with the operating theater) and demonstrating benefits in meaningful outcomes as a result of continuous, objective monitoring.

## Competing interests

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