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Monitoring of sedation in mechanically ventilated patients using remote technology

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Abstract

Purpose of review—Two years of COVID-19 pandemic highlighted that excessive sedation in the ICU leading to coma and other adverse outcomes remains pervasive. There is a need to improve monitoring and management of sedation in mechanically ventilated patients. Remote technologies that are based on automated analysis of EEG could enhance standard care and alert clinicians real-time when severe EEG suppression or other abnormal brain states are detected.

Recent findings—High rates of drug-induced coma as well as delirium were found in several large cohorts of mechanically ventilated patients with COVID-19 pneumonia. In patients with ARDS, high doses of sedatives comparable to general anesthesia have been commonly administered without defined EEG endpoints. Continuous limited-channel EEG can reveal pathologic brain states such as burst suppression, that cannot be diagnosed by neurological examination alone. Recent studies documented that machine learning-based analysis of continuous EEG signal is feasible and that this approach can identify burst suppression as well as delirium with high specificity.

Summary—Preventing oversedation in the ICU remains a challenge. Continuous monitoring of EEG activity, automated EEG analysis, and generation of alerts to clinicians may reduce drug-induced coma and potentially improve patient outcomes.

Keywords

COVID-19; sedation; acute respiratory distress syndrome; burst suppression; electroencephalography

Introduction

Pharmacological sedation is a complex medical intervention that is delivered to most mechanically ventilated patients in the ICUs [1]. Multiple aspects of sedation, including the choice of drug(s), their dose, the mode of administration (continuous vs. intermittent),

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the desired level of sedation, and the interruptions of sedation need to be individualized to ensure patient comfort, safety, and optimal outcomes [2, 3].

Continuous reassessment of sedation strategy is required as patient's primary problem evolves (e.g., worsening ARDS), or patients develop new end-organ dysfunction (liver, renal, heart failure) that alters drug metabolism. Sedation of obese, morbidly obese, and elderly patients, who are highly represented in the ICUs in the United States, may require careful adjustments in dosing due to alterations in pharmacokinetics, but there is a paucity of data on sedation in these patient groups [4, 5]. Finally, in contrast to brief anesthetics administered in the operating room, sedation in the ICU is typically delivered over prolonged periods which further impacts pharmacokinetics, and also results in tolerance to these agents [6, 7]. Given this complexity of sedation management, it is difficult to justify why most sedation in the ICUs is administered without monitoring the target organ – brain – with electroencephalogram (EEG), and sedation is titrated based on clinical assessments alone.

Intermittent assessments may be sufficient in those patients who tolerate mechanical ventilation while being awake or lightly sedated and respond to verbal stimulation (RASS −3 to 0). However, repeat clinical assessments over longer periods could also be detrimental if they interrupt patient's sleep. When deeper sedation (RASS −4 to −5) is deemed necessary (e.g., in some patients with severe ARDS), clinical assessments are less reliable as they cannot distinguish between appropriate sedation depth (EEG characterized by slow delta waves) and excessive sedation depth (EEG characterized by burst suppression or isoelectricity) [8, 9]. With sedation depth also likely to fluctuate, prolonged periods of coma may be left undetected in between clinical assessments.

The widespread practice of administering sedation without clear EEG endpoints is concerning, given that excessive sedation has been associated with many adverse outcomes. Deep sedation prolongs mechanical ventilation (and inevitably patient immobilization) as well as ICU stay [10–12]. Prolonged ventilation could increase complications such as ventilator-associated pneumonia and ICU-acquired weakness [13, 14]. Several recent studies found links between adverse brain states (burst suppression, coma) and mortality [15*, 16*]. Relationships between deep sedation in the ICU and subsequent sleep abnormalities, delirium, cognitive dysfunction, functional decline, and mortality, require further investigation [17–19, 20*, 21]. Finally, significant complications such as ischemic and hemorrhagic stroke could be masked by deep sedation, as illustrated in a recent case series of patients with severe COVID-19 ARDS [22]. Because of these potentially important impacts of sedation on outcomes, 2018 PADIS (Pain, Agitation/Sedation, Delirium, Immobility, Sleep Disruption) guidelines recommended that light sedation should be pursued in mechanically ventilated patients whenever feasible [2, 23].

We propose that a broader adoption of limited-channel EEG monitoring in the medical and surgical ICUs could increase the timely detection of oversedation (burst suppression, isoelectricity) and provide objective data to clinicians when adjusting sedation dosing. Limited channel EEG sensors are widely available and routinely used in operating rooms where the interpretation of EEG signal relies on the expertise of anesthesiologist. EEG

facilitates titration of both inhalational and intravenous anesthetics during surgery so that excessive anesthetic depth or inadequate anesthesia (and possibly awareness) can be avoided [24–26]. However, it is not feasible for anesthesiologists or neurologists to be continuously present at the bedside in the ICUs or review EEGs of large numbers of ventilated patients remotely. Remote technology solutions where continuous EEG is analyzed in an automated manner, and important alerts (e.g., burst suppression, isoelectricity, nonconvulsive seizures) are sent in real time to clinicians, may facilitate adoption of continuous EEG monitoring in non-neurologic ICUs. Recent studies documented that automated tracking of sedation, sleep and delirium using machine learning is feasible. These computational advancements will allow more precise quantitation of abnormal brain states and potentially improve clinical care in the future.

Deep sedation and coma remain common in mechanically ventilated patients

These last two years of COVID-19 pandemic documented that acute neurologic dysfunction (e.g., coma, delirium) remains common in mechanically ventilated patients, that sedation of patients with respiratory failure continues to pose multiple challenges to ICU clinicians, and adherence to several components of ICU Liberation (ABCDEF) bundle may be suboptimal.

Pun et al studied 2088 patients with COVID-19 ARDS across multiple institutions and found that over 80% patients were comatose at some point during their ICU stay [27**]. Median duration of coma was 10 days. Delirium was present in over 50% patients, with a median duration of 3 days. In this cohort, 64% of patients were exposed to benzodiazepines, and a benzodiazepine infusion was strongly associated with delirium. Wongtangman et al studied a population of 114 mechanically ventilated patients with COVID-19, most of which had mild-to-moderate ARDS [15*]. They found that out of the first 10 days of ventilation, 66±31.3% days were spent in coma, and the hypnotic agent dose was associated with coma. The median daily dose of propofol was 3606 mg, which was a significantly higher dose when compared to 1773 mg in a matched non-COVID ARDS cohort.

Our analysis of a smaller COVID-19 ARDS cohort found a similarly high exposure to propofol (mean of 52,151 mg for the duration of ICU stay) [28*], and these doses were 2–3-fold higher when compared to historical non-COVID ICU cohorts from our institution [16]. Balakrishna et al analyzed sedation exposure in a cohort of 86 mechanically ventilated patients with COVID-19 ARDS [29]. The authors found that median RASS score during each of the first 10 days of ventilation was −4, and the number of sedative drug agents administered simultaneously increased over time. Propofol and hydromorphone infusions were the most commonly used sedatives (up to 100% and 88% patients on any given day, respectively). By day 10, almost 50% patients were also receiving midazolam.

Despite these extraordinary exposures to sedatives and analgesics, the use of continuous EEG to monitor sedation was not reported in these cohort studies.

High rates of coma were recently found in cohorts of critically ill patients with other diseases than COVID-19. Hogan et al studied the prevalence of burst suppression, a

pathological EEG pattern characterized by high amplitude “bursts” alternating with periods of low or flatline “suppression”, in critically ill patients with various primary diagnoses [16**]. Out of 471 adult mechanically ventilated patients in their cohort, 238 (50.5%) patients experienced some degree of burst suppression that was not intentional. Sixty-three patients (13.4%) were in burst suppression almost the entire time that the EEG was recorded. While the authors estimated that burst suppression burden increases with high propofol exposure, burst suppression was primarily attributed to critical illness itself. The authors proposed that burst suppression may serve as a biomarker of medical and neurologic “vulnerability”, and that the administration of propofol and other sedatives might need to be more judicious in these vulnerable patients.

Given that both 2013 PAD and 2018 PADIS guidelines recommended light sedation in mechanically ventilated patients, it is important to understand potential barriers to maintaining best sedation practices, and iatrogenic factors leading to coma. Others and we proposed that certain factors specific to COVID-19 pandemic may have led to oversedation in the ICUs over the last two years, including: i) prolonged mechanical ventilation in COVID-19 ARDS and prolonged administration of sedative infusions, ii) use of higher amounts of hypnotics and opioids to limit ventilator dyssynchrony despite ample evidence that deep sedation may worsen rather than improve ventilator dyssynchrony, iii) use of paralysis and therefore deeper levels of sedation, iiii) reduced frequency of spontaneous awakening and breathing trials in patients with COVID-19 ARDS due to concerns over respiratory decompensation, iiiii) increased use of benzodiazepines (e.g., midazolam) to escalate sedation in patients tolerant to sedatives, or in the setting of ICU drug shortages, and iiiiii) increased prevalence of obese and morbidly obese patients being treated (and actual weight-based drug dosing) [7, 15, 30, 31].

Investigators in the field of nursing recently identified additional factors leading to suboptimal adherence with ABCDEF bundle. In a study of 977 mechanically ventilated patients treated in 15 ICUs in the western part of United States, the highest overall adherence to the bundle was found in patients requiring less than 48 hours of ventilation, and adherence to individual components of bundle (except spontaneous breathing trials and delirium) was associated with number of days on mechanical ventilation. Delirium assessments were performed with the lowest frequency in Hispanic patients, likely due to communication barrier. Although authors studied only the first 96 hours of ventilation, these results suggest that the elements of the A-F bundle are less likely to be performed as the duration of ventilation increases, i.e., in sicker patients, and in certain ethnic groups [32].

Anderson et al recently proposed that sedation assessment by ICU nurses may be vulnerable to “care erosion” – i.e., deterioration of skills over time. In a small, single center medical ICU cohort, the usual care nursing assessments resulted in significantly higher RASS scores when compared with corresponding, script-driven protocolized RASS assessments. Authors postulate that these assessment discrepancies, i.e., not recognizing when patient is comatose, may contribute to patient oversedation in the ICUs [33].

Rubulotta et al suggested that broader adoption of technologies may optimize care of mechanically ventilated patients with COVID-19, especially when health care providers are

challenged by limited resources. For example, authors advocate for increased utilization of processed EEG to guide sedation, however, the issue of EEG interpretation (and possible misinterpretation) by ICU staff who oftentimes have limited knowledge of EEG, is not fully addressed [34]. Moreover, the interpretation of EEG in the ICU may be more challenging than in the operating room due to polypharmacy and effects of critical illness (e.g., septic encephalopathy, delirium).

Michalak et al investigated whether sedation of patients with severe COVID-19 ARDS who were also receiving paralytics could be aided by limited frontotemporal EEG, interpreted daily by epileptologist. In this cohort, the EEG pattern was found to be severely suppressed on 58% days. The expert EEG review was followed by recommendations to decrease sedation (in cases of severe EEG suppression) or maintain sedation (in cases of adequate EEG pattern), which were largely followed by the ICU team. Given the small numbers of treated patients (n=11), it was not possible to determine whether this approach had any impact on patient outcomes [35].

Automated tracking of sedation, delirium and sleep with EEG is feasible

There is ample evidence that clinical bedside evaluations have limitations when assessing depth of sedation, presence and severity of delirium, and presence and quality of sleep in the ICU. Even if performed carefully, these evaluations are intermittent, based on observed patient behaviors, and there is inter-observer variability. Oversedation and delirium are therefore commonly underdiagnosed, and the duration of coma, delirium or sleep are not recorded accurately. However, the precise detection of these abnormal brain states and of the sleep in the ICU may be important as they impact short-term outcomes (e.g., length of ventilation, success of extubation, length of ICU stay), and potentially long-term outcomes (e.g., survival, cognitive function).

There are actions that could be taken in the ICU when new brain dysfunction is detected – e.g., cessation of all sedatives, avoidance of benzodiazepines, reduction of opioids, or sleep promoting measures. There is therefore a need to enhance clinical evaluation with objective measures of brain dysfunction and make these assessments continuous throughout the ICU stay and possibly beyond the ICU.

EEG is an objective signal which reflects both structural and functional changes of the brain with excellent temporal resolution [36, 37]. The practice of continuous EEG recording is common in neurologic ICUs, where full montage EEG is used to identify non-convulsive seizures, non-convulsive status epilepticus, and cerebral ischemia. However, continuous EEG is labor -intensive as it requires remote review by neurophysiologist at least twice daily. Automated seizure detection algorithms can streamline the analysis by highlighting those parts of the EEG record where seizures are most likely. Near real-time alerts are available on some platforms and can notify clinicians when seizure is suspected. To facilitate remote seizure monitoring in ambulatory patients, wireless wearable miniature EEG sensors have been developed [38].

We propose that these technological advancements of tele-neurology could also be applied in mechanically ventilated patients to allow consciousness, delirium, and sleep tracking. First, the use of unobtrusive wireless EEG sensors will allow usual nursing care (patient positioning, proning) without limiting patient movement. Second, continuous, and automated analysis using machine learning could increase detection of abnormal brain states which cannot be identified clinically (e.g., burst suppression, nonconvulsive seizures). Third, generation of automated alerts will prompt clinicians to evaluate patients at the bedside when abnormality is detected [39, 40] (Figure 1)

Several recent studies used supervised and unsupervised machine learning to automate EEG analysis, and these approaches achieved good performance. Sun et al developed deep learning model based on convolutional and recurrent neural networks that continuously tracks level of consciousness and delirium from four-channel frontal EEG. The model was trained using preprocessed EEG waveforms, RASS and CAM-ICU assessments that were obtained from mechanically ventilated patients with various primary diagnoses and receiving various combinations of sedatives. For the level of consciousness, the system achieved accuracy comparable to clinical observers, and delirium was predicted with AUC of 0.80 with 69% sensitivity and 83% specificity [41].

Narula et al. created unsupervised burst suppression detection algorithm for quantitative assessment of coma depth (bursts per minute) in patients receiving deep sedation. The goal of the algorithm is to facilitate precise sedation and eliminate variability in assessing sedation depth by clinicians. Authors found that a mean absolute error in estimating bursts-per-minute by the algorithm was approximately one burst, which would not be an important error in clinical practice. The performance of their unsupervised algorithm was comparable with a more advanced neural network model [42].

Van Sleuwen et al used machine learning to predict presence and severity of delirium (EEG Confusion Assessment Method severity score; E-CAM-S score) in a heterogeneous ICU population (n=373) based on four frontal EEG channels. Severity of delirium was associated with more EEG slowing (increased delta content, reduced alpha content), and E-CAM-S score correlated well with clinical CAM-S as well as with in-hospital mortality [43*].

Sleep architecture can be profoundly changed by critical illness leading to the reduction or complete absence of deep sleep (slow wave sleep, stage 3 NREM sleep) and REM sleep, while proportion of light sleep (stage 1 and 2 NREM) may be increased. Benzodiazepines and opioids may also suppress slow wave sleep and REM sleep. The extent to which the altered sleep is detrimental in critically ill patients is largely unknown, but the consequences likely include cognitive, respiratory, and immune cell dysfunction [44]. For example, in a study of mechanically ventilated patients using polysomnography, altered sleep (i.e., atypical sleep or no REM sleep) was found in 44% patients and was associated with longer ventilation weaning [45].

Clinical sleep evaluations in mechanically ventilated patients are inaccurate, hampered by sedation and delirium, and are not performed consistently outside of research studies. Boyko et al found that nursing assessments of sleep in mechanically ventilated patients with COPD

and sepsis do not correlate with polysomnography when atypical sleep is present. In their study, patients experiencing atypical sleep were similarly likely to be assessed as either “awake” or “asleep” by a bedside nurse [46]. Automated sleep stage classification from EEG data using artificial intelligence is therefore crucial to enable accurate sleep tracking in the ICU.

Sun et al developed automated sleep staging algorithm trained on large-scale EEG data sets from 1000 patients undergoing routine polysomnography which was validated on another 1000 testing patients. The algorithm performed favorably when compared to human scorers (inter-rater reliability of 0.63) [47]. Biswal et al trained deep recurrent convolutional neural network with 10,000 clinical polysomnographs. The model achieved accuracy comparable to human experts in scoring sleep stages, sleep apnea events, and limb movements. Of note, training on limited EEG channels (to mimic at-home wearable EEG devices) resulted in only a small reduction in accuracy [48].

A proposed workflow to enhance sedation monitoring in mechanically ventilated patients

High rates of burst suppression and coma have been detected in cohorts of mechanically ventilated patients, and especially those with ARDS. To reduce the rates of inadvertent coma, we propose that some additional measures which would supplement widely adopted 2018 PADIS guidelines can be taken at the bedside:

1. Application of limited-channel frontal EEG sensor (preferably wireless) and recording of brief EEG baseline before administering anesthetics for endotracheal intubation. Baseline EEG may reveal features of vulnerable brain (e.g., reduced frontal alpha power), signaling a patient at risk [49].
2. Early interruption of sedation after the effect of paralytics used for intubation wears off. A careful trial of no sedation/light sedation (RASS goal −2 to 0) should be performed early during mechanical ventilation, before sedation-related encephalopathy or delirium/agitation develop.
3. Intermittent (e.g., every 12 hours) examination of EEG spectrogram and real-time raw EEG by intensivist in patients receiving deep sedation, with the goal to identify accidental burst suppression or isoelectricity (easy to recognize patterns). Alternatively, an automated and continuous EEG analysis with alerts sent to clinicians when burst suppression/coma is identified.
4. Interruption/decrease of sedative infusions whenever burst suppression/coma are identified on EEG. Frequent assessments of the patient until responsiveness to verbal stimulation is regained. Individualized work-up (brain imaging, liver, and renal function tests) if responsiveness is not regained.
5. No escalation of sedation in patients who have ventilator dyssynchrony and are already deeply sedated (RASS −3 and lower). There is an ample evidence that drug-induced coma may worsen, rather than improve dyssynchrony. Coma promotes ineffective triggering and reverse triggering. In deeply sedated patients,

ventilator dyssynchrony should be treated by adjusting ventilator settings (e.g. increasing inspiratory flow, increasing inspiratory time), and if feasible, by lightening sedation [3].

6. Daily documentation of EEG spectrograms and 24-hour cumulative sedation exposure in medical records, or research database, for quality improvement and research purposes.

Conclusion

There is increasing evidence that deep sedation and delirium increase duration of mechanical ventilation and mortality. The quantities of sedation, the duration of delirium, and the duration and stages of sleep are important variables that affect the outcomes of mechanically ventilated patients. In current clinical practice, depth of sedation, delirium, and sleep are assessed by clinicians at the bedside; however, these clinical assessments are intermittent, and can be inaccurate as they are reflective of patient behavior rather than the underlying neurophysiology. Continuous monitoring with limited channel EEG could supplement clinical evaluations and provide objective and real-time information on brain function. Machine learning algorithms can be trained to recognize coma, delirium, and stages of sleep and these technological advancements will reduce the need for an expert EEG interpretation at the bedside.

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References and recommended reading

1. Skivington K, Matthews L, Simpson SA, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ 2021;374:n2061. [PubMed: 34593508]
2. Devlin JW, Skrobik Y, Gélinas C, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med 2018;46(9):e825–e873. [PubMed: 30113379]
3. Chanques G, Constantin JM, Devlin JW, et al. Analgesia and sedation in patients with ARDS. Intensive Care Med 2020;46(12):2342–2356. [PubMed: 33170331]
4. Erstad BL, Barletta JF. Drug dosing in the critically ill obese patient-a focus on sedation, analgesia, and delirium. Crit Care 2020;24(1):315. [PubMed: 32513237]
5. Mukhopadhyay A, Tai BC, Remani D, et al. Age related inverse dose relation of sedatives and analgesics in the intensive care unit. PLoS One 2017;12(9):e0185212. [PubMed: 28957364]

6. Tse AHW, Ling L, Lee A, Joynt GM. Altered Pharmacokinetics in Prolonged Infusions of Sedatives and Analgesics Among Adult Critically Ill Patients: A Systematic Review. Clin Ther 2018;40(9):1598–1615.e2. [PubMed: 30173953]

7. Hanidziar D, Bittner EA. Sedation of Mechanically Ventilated COVID-19 Patients: Challenges and Special Considerations. Anesth Analg 2020;131(1):e40–e41. [PubMed: 32392023]

8. Edlow BL, Claassen J, Victor JD, et al. Delayed reemergence of consciousness in survivors of severe COVID-19. Neurocrit Care 2020;33(3):627–629. [PubMed: 33174149]

9. Purdon PL, Sampson A, Pavone KJ, Brown EN. Clinical Electroencephalography for Anesthesiologists: Part I: Background and Basic Signatures. Anesthesiology 2015;123(4):937–60. [PubMed: 26275092]

10. Shehabi Y, Bellomo R, Reade MC, et al. ; Sedation Practice in Intensive Care Evaluation (SPICE) Study Investigators; ANZICS Clinical Trials Group. Early intensive care sedation predicts long-term mortality in ventilated critically ill patients. Am J Respir Crit Care Med 2012;186(8):724–31. [PubMed: 22859526]

11. Shehabi Y, Chan L, Kadiman S, et al. ; Sedation Practice in Intensive Care Evaluation (SPICE) Study Group investigators. Sedation depth and long-term mortality in mechanically ventilated critically ill adults: a prospective longitudinal multicentre cohort study. Intensive Care Med 2013;39(5):910–8. [PubMed: 23344834]

12. Shehabi Y, Bellomo R, Kadiman S, et al. ; Sedation Practice in Intensive Care Evaluation (SPICE) Study Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group. Sedation Intensity in the First 48 Hours of Mechanical Ventilation and 180-Day Mortality: A Multinational Prospective Longitudinal Cohort Study. Crit Care Med 2018;46(6):850–859. [PubMed: 29498938]

13. Weinberger J, Cocoros N, Klompas M. Ventilator-Associated Events: Epidemiology, Risk Factors, and Prevention. Infect Dis Clin North Am 2021; 35(4):871–899. [PubMed: 34752224]

14. Vanhorebeek I, Latronico N, Van den Berghe G. ICU-acquired weakness. Intensive Care Med 2020;46(4):637–653. [PubMed: 32076765]

15*. Wongtangman K, Santer P, Wachtendorf LJ, et al. ; SICU Optimal Mobilization Team (SOMT) Group. Association of Sedation, Coma, and In-Hospital Mortality in Mechanically Ventilated Patients With Coronavirus Disease 2019-Related Acute Respiratory Distress Syndrome: A Retrospective Cohort Study. Crit Care Med 2021;49(9):1524–1534. [PubMed: 33861551] A retrospective study which documents that high exposures to sedatives in patients with COVID-19 ARDS was associated with coma and mortality.

16*. Hogan J, Sun H, Aboul Nour H, et al. Burst Suppression: Causes and Effects on Mortality in Critical Illness. Neurocrit Care 2020;33(2):565–574. [PubMed: 32096120] This study documents high prevalence of burst suppression on EEGs in a cohort of mechanically ventilated patients.

17. Mart MF, Pun BT, Pandharipande P, et al. ICU Survivorship-The Relationship of Delirium, Sedation, Dementia, and Acquired Weakness. Crit Care Med 2021;49(8):1227–1240. [PubMed: 34115639]

18. Rengel KF, Hayhurst CJ, Pandharipande PP, Hughes CG. Long-term Cognitive and Functional Impairments After Critical Illness. Anesth Analg 2019;128(4):772–780. [PubMed: 30883422]

19. Hayhurst CJ, Marra A, Han JH, et al. Association of Hypoactive and Hyperactive Delirium With Cognitive Function After Critical Illness. Crit Care Med 2020;48(6):e480–e488. [PubMed: 32317589]

20*. Duprey MS, Dijkstra-Kersten SMA, Zaal IJ, et al. Opioid Use Increases the Risk of Delirium in Critically Ill Adults Independently of Pain. Am J Respir Crit Care Med 2021;204(5):566–572. [PubMed: 33835902] This study documents that opioids increase the odds of delirium in the ICU in a dose-dependent fashion.

21. Trompeo AC, Vidi Y, Locane MD, et al. Sleep disturbances in the critically ill patients: role of delirium and sedative agents. Minerva Anestesiol 2011;77(6):604–12. [PubMed: 21617624]

22. Bruce SS, Kahan J, Huq T, et al. Missed cerebrovascular events during prolonged sedation for COVID-19 pneumonia. J Clin Neurosci 2021;86:180–183. [PubMed: 33775324]

23. Devlin JW, Seth B, Train S, Needham DM. Maintaining light sedation is important: next steps for research. Thorax 2021;76(11):1069–1070. [PubMed: 34272337]

24. Romagnoli S, Franchi F, Ricci Z. Processed EEG monitoring for anesthesia and intensive care practice. Minerva Anestesiol 2019;85(11):1219–1230. [PubMed: 31630505]
25. Scheeren TWL, Kuizenga MH, Maurer H, et al. Electroencephalography and Brain Oxygenation Monitoring in the Perioperative Period. Anesth Analg 2019;128(2):265–277. [PubMed: 29369096]
26. Massari D, de Keijzer IN, Scheeren TWL. Cerebral monitoring in surgical ICU patients. Curr Opin Crit Care 2021;27(6):701–708. [PubMed: 34475324]
27**. Pun BT, Badenes R, Heras La Calle G, et al. ; COVID-19 Intensive Care International Study Group. Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): a multicentre cohort study. Lancet Respir Med 2021;9(3):239–250. [PubMed: 33428871] A multi-center study which documents high prevalence of coma and delirium in patients with COVID-19 ARDS, and strong association of benzodiazepine infusion with delirium.
28*. Hanidziar D, Baldyga K, Ji CS, et al. Standard Sedation and Sedation With Isoflurane in Mechanically Ventilated Patients With Coronavirus Disease 2019. Crit Care Explor 2021;3(3):e0370. [PubMed: 33786446] This study documents the use of anesthesia machines to provide mechanical ventilation and sedation with isoflurane in patients with COVID-19 ARDS.
29. Balakrishna A, Walsh EC, Hamidi A, et al. An examination of sedation requirements and practices for mechanically ventilated critically ill patients with COVID-19. Am J Health Syst Pharm 2021;78(21):1952–1961. [PubMed: 33993212]
30. de Haro C, Magrans R, López-Aguilar J, et al. ; Asynchronies in the Intensive Care Unit (ASYNICU) Group. Effects of sedatives and opioids on trigger and cycling asynchronies throughout mechanical ventilation: an observational study in a large dataset from critically ill patients. Crit Care 2019;23(1):245. [PubMed: 31277722]
31. Vaschetto R, Cammarota G, Colombo D, et al. Effects of propofol on patient-ventilator synchrony and interaction during pressure support ventilation and neurally adjusted ventilatory assist. Crit Care Med 2014;42(1):74–82. [PubMed: 23982026]
32. DeMellow JM, Kim TY, Romano PS, et al. Factors associated with ABCDE bundle adherence in critically ill adults requiring mechanical ventilation: An observational design. Intensive Crit Care Nurs 2020;60:102873. [PubMed: 32414557]
33. Anderson CC, Johnson JL, deBoisblanc BP, Jolley SE. Care erosion in sedation assessment: A prospective comparison of usual care Richmond Agitation-Sedation Scale assessment with protocolized assessment for medical intensive care unit patients. J Nurs Manag 2021;29(2):206–213. [PubMed: 32881119]
34. Rubulotta F, Soliman-Aboumarie H, Filbey K, et al. Technologies to Optimize the Care of Severe COVID-19 Patients for Health Care Providers Challenged by Limited Resources. Anesth Analg 2020;131(2):351–364. [PubMed: 32433248]
35. Michalak AJ, Mendiratta A, Eliseyev A, et al. Frontotemporal EEG to guide sedation in COVID-19 related acute respiratory distress syndrome. Clin Neurophysiol 2021;132(3):730–736. [PubMed: 33567379]
36. Herman ST, Abend NS, Bleck TP, et al. ; Critical Care Continuous EEG Task Force of the American Clinical Neurophysiology Society. Consensus statement on continuous EEG in critically ill adults and children, part I: indications. J Clin Neurophysiol 2015;32(2):87–95. [PubMed: 25626778]
37. Katyal N, Singh I, Narula N, et al. Continuous Electroencephalography (CEEG) in Neurological Critical Care Units (NCCU): A Review. Clin Neurol Neurosurg 2020;198:106145. [PubMed: 32823186]
38. Frankel MA, Lehmkuhle MJ, Spitz MC, et al. Wearable Reduced-Channel EEG System for Remote Seizure Monitoring. Front Neurol 2021;12:728484 [PubMed: 34733229]
39. Byrom B, McCarthy M, Schueler P, Muehlhausen W. Brain Monitoring Devices in Neuroscience Clinical Research: The Potential of Remote Monitoring Using Sensors, Wearables, and Mobile Devices. Clin Pharmacol Ther 2018;104(1):59–71. [PubMed: 29574776]
40. Baldassano SN, Roberson SW, Balu R, et al. IRIS: A Modular Platform for Continuous Monitoring and Caretaker Notification in the Intensive Care Unit. IEEE J Biomed Health Inform 2020;24(8):2389–2397. [PubMed: 31940568]

41. Sun H, Kimchi E, Akeju O, et al. Automated tracking of level of consciousness and delirium in critical illness using deep learning. NPJ Digit Med 2019;2:89. [PubMed: 31508499]

42. Narula G, Haeberlin M, Balsiger J, et al. Detection of EEG burst-suppression in neurocritical care patients using an unsupervised machine learning algorithm. Clin Neurophysiol 2021;132(10):2485–2492. [PubMed: 34454277]

43*. van Sleuwen M, Sun H, Eckhardt C, et al. Physiological Assessment of Delirium Severity: The Electroencephalographic Confusion Assessment Method Severity Score (E-CAM-S). Crit Care Med 2022;50(1):e11–e19. [PubMed: 34582420] In this study, machine learning was utilized to analyze EEG signal and predict delirium severity.

44. Telias I, Wilcox ME. Sleep and Circadian Rhythm in Critical Illness. Crit Care 2019;23(1):82. [PubMed: 30850003]

45. Thille AW, Reynaud F, Marie D, et al. Impact of sleep alterations on weaning duration in mechanically ventilated patients: a prospective study. Eur Respir J 2018;51(4):1702465. [PubMed: 29519925]

46. Boyko Y, Jennum P, Oerding H, et al. Sleep in critically ill, mechanically ventilated patients with severe sepsis or COPD. Acta Anaesthesiol Scand 2018. doi: 10.1111/aas.13140. Epub ahead of print.

47. Sun H, Jia J, Goparaju B, et al. Large-Scale Automated Sleep Staging. Sleep. 2017;40(10):zsx139. doi:10.1093/sleep/zsx139.

48. Biswal S, Sun H, Goparaju B, et al. Expert-level sleep scoring with deep neural networks. J Am Med Inform Assoc 2018;25(12):1643–1650. [PubMed: 30445569]

49. Shao YR, Kahali P, Houle TT, et al. Low Frontal Alpha Power Is Associated With the Propensity for Burst Suppression: An Electroencephalogram Phenotype for a “Vulnerable Brain”. Anesth Analg 2020; 131(5):1529–1539. [PubMed: 33079876]

Key points:

1. EEG monitoring in medical and surgical ICU patients will be increasingly available through advancements in hardware design (e.g., wireless sensors) which allow continuous data collection and patient mobility
2. Machine learning models can be trained to detect coma, delirium, and sleep stages from EEG and generate alerts to clinicians when important abnormalities are detected
3. Automated detection and accurate quantitation of abnormal brain states will be crucial to study the impact of coma, delirium, and abnormal sleep on outcomes of mechanically ventilated patients

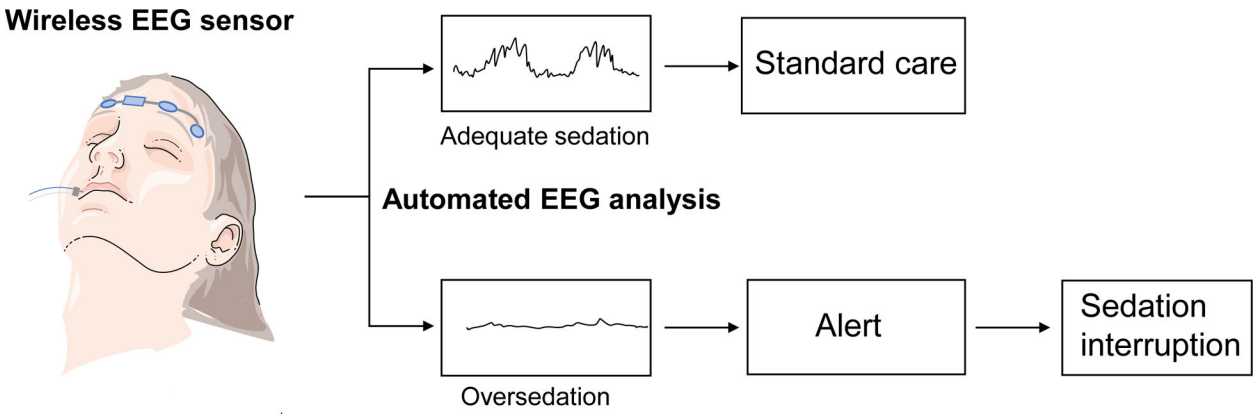

Figure. Automated EEG analysis for remote sedation monitoring.

When adequate levels of sedation (delta waves) are detected, a standard sedation care can continue. When excessive levels of sedation (burst suppression, isoelectricity) are detected, alerts to the clinician can be issued, and a decrease in sedation can be considered. Components of this figure were created using Servier Medical Art templates, which are licensed under a Creative Commons Attribution 3.0 Unported License; https://smart.servier.com.