Chapter

# The Challenges of EEG in Coma: The Potential of Recent Discoveries

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## Abstract

The utilization of electroencephalography (EEG) has profoundly enriched our comprehension and monitoring of patients, especially those in intensive care units (ICUs), over the past decades. EEG, a method of recording electrical brain signals, is employed to explore a variety of neurological disorders such as epilepsy, dementia, and brain injuries that may affect unconscious patients. In recent years, EEG has also been used to monitor sedation levels, examine the quality of patients' sleep, and track patient recovery during periods of coma. Groundbreaking findings, derived from EEG recordings in intensive care using various techniques and methodologies, have unveiled new avenues to aid these patients and improve physicians' understanding of their condition and needs. Innovations such as the examination of sleep quality, the assessment of pain and stress, and the classification of vigilance states represent some of the promising advancements in ICUs, all of which are based on EEG. Recent discoveries stemming from EEG signal analysis have indicated numerous potential enhancements in improving comfort, fostering a better understanding of the situation, and reducing the administration of drugs for ICU patients. In this chapter, we will discuss some new EEG findings for intensive care unit patients and the possible applications that could be revealed based on other investigations on human subjects outside the ICU.

**Keywords:** coma, ICU, EEG, artifact removal, sedation, sleep quality, pain assessment, stress investigation

## 1. Introduction

EEG is the recording of electrical brain activity through electrodes placed on the human scalp. This method was published for the first time by a German psychiatrist named Hans Berger (1873–1941) in 1929 [1] after 4 years of electrical recordings of human brain activity. A few years later, the results were confirmed by Edgar Adrian (1889–1977). Since then, EEG research has been used to investigate epilepsy, brain tumors, sleep quality, and the involvement of brain areas in human body functions [2]. In the medical field, the duration of EEG recording varies from a minimum of 20 minutes–72 hours. A recording that exceeds 24 hours is called continuous EEG (cEEG) and is the main recording method in the intensive care unit (ICU).

This technique is used to investigate and control abnormal activities in the brain of a subject, monitor patient improvement during the coma period, and monitor sedation, among other applications. Admission to the ICU can have a substantial effect on the patient's condition. This could potentially result in exposure to numerous painful stimuli and increased stress levels due to various factors, which could subsequently induce anxiety. Taken together, these factors could contribute to sleep deprivation in patients.

Medical professionals strive to mitigate the effects of coma such as stress, severe pain, and sleep deprivation that could complicate the patient's situation and delay recovery. These effects could be detected through either electronic monitoring by electrical machines connected to the patient's body or behavioral and physiological assessments by means of a number of scores used on ICU patients or by observation. Doctors have been trying to reduce these effects primarily by using pharmacological interventions. Although these medications can alleviate the symptoms mentioned above, they can also introduce side effects that could further complicate the patient's condition.

Stress is a response of the human body to external challenges, pressures, or stimuli that can cause physical, emotional, or mental disturbances [3]. It can manifest itself in two forms: positive and negative. Positive stress, also known as "eustress," helps us avoid danger by keeping us alert and prepared. On the other hand, negative stress, referred to as "distress," is associated with numerous health complications [4]. The experience of stress varies significantly between individuals. According to [5], stress can be categorized into three types: mental stress, emotional stress, and physical stress.

In response to stress, the human body undergoes physiological reactions. Hormones such as adrenaline and cortisol are released by the sympathetic nervous system to prepare the body for an emergency. This reaction triggers physical symptoms, including an accelerated heartbeat, increased blood pressure, rapid breathing, and heightened senses [6]. If this automatic bodily response reaches an excessively high level of intensity, it can lead to mental and/or physical health issues. The effects of these issues can become evident in the individual's future, especially in affecting their productivity and quality of life [7]. Stress, a significant consequence of being in a coma, should be investigated and treated correctly to avoid further complications in patients' conditions. EEG was found to be useful in investigating stress in ICU patients. The latest research funding of EEG in the stress investigation will be further discussed in Section 3.2.

Stress is not the sole repercussion experienced by comatose patients. Pain, whether resulting from injury or medical treatment, also poses a significant challenge in the ICU. Given the patients' diminished consciousness levels during the coma, they are unable to communicate their pain experiences. Consequently, medical professionals have developed various pain scales to evaluate pain intensity, relying on a range of behavioral and physiological patient responses. These scores were very limited, especially in the case of sedative drug injection [8]. On the other hand, excessive usage of sedative drugs can affect the recovery of the comatose patient; therefore, more investigation for new methods to assess pain in the ICU is needed. EEG could be one of the solutions to overcome these limitations based on new findings that we will discuss in Section 4.2.

The two aforementioned issues that a patient in a coma may encounter in the ICU could result in sleep deprivation. In fact, poor sleep quality can cause discomfort and exacerbate the patient's stress and pain levels [9].

A typical sleep cycle comprises three stages of non-REM sleep (N1, N2, N3), followed by REM sleep. A sleep cycle lasts about 90 minutes in adults. Rapid eye movement (REM) sleep is essential for brain development, emotions, and memory processing [10]. Optimal sleep quality is achieved with four to five of these cycles. However, in the ICU, patients often experience sleep deprivation due to a multitude of factors, which will be discussed in Section 3.1. Several methods have been developed to assess sleep quality in intensive care unit patients. Polysomnography (PSG) is a comprehensive technique that uses simultaneous physiological and electrical recordings, including EEG, EOG, EMG, and ECG, to provide a standard measurement [11]. Emerging technologies, such as smartwatches and under-bed sensors, are being explored for the assessment of sleep quality, although they have not yet been validated or widely adopted in large-scale studies. However, other scales such as the Bispectral Index (BIS) and the Richards-Campbell Sleep Questionnaire (RCSQ) may not be reliable for critically ill patients or those with low levels of consciousness [12]; therefore, researchers have begun investigating EEG with different classifier methods to determine sleep stages and evaluate sleep quality. Section 3.1 will deal with details of this field.

One of the most important scales in the ICU is the vigilance scale, a physiological-based stimuli response score that helps specialists understand how aware the comatose patient is. One of the most widely used scores is the Glasgow Coma scale [13]. This score is based on three different types of stimuli response: verbal, motor, and eye movement response. This score and its given points are detailed in **Table 1**. A comatose patient is a patient with a GCS equal to or under 8. Other scores have been invented all over the world, but no one has overcome the GCS score. Coma scales have been identified as limited for various reasons, including physical disabilities, sedative drug injection, mental disorders, and alcohol consumption before admission. The

| Stimuli | Response | Points |
|---|---|---|
| | No response | 1 |
| Eyes response | Only to pain | 2 |
| | To stimuli | 3 |
| | Spontaneous | 4 |
| | No response | 1 |
| Verbal response | Incomprehensible speech | 2 |
| | Inappropriate words | 3 |
| | Confused conversation | 4 |
| | Oriented | 5 |
| | No response | 1 |
| Motor response | Extension | 2 |
| | Flexion | 3 |
| | Withdraws | 4 |
| | Purposeful movement | 5 |
| | Obeys commands to movement | 6 |

**Table 1.**
*The Glasgow coma scale (GCS).*

| Brain wave | Frequency band (Hz) |
|---|---|
| Delta ( $\delta$ ) | 1–4 |
| Theta ( $\theta$ ) | 4–8 |
| Alpha ( $\alpha$ ) | 8–13 |
| Beta ( $\beta$ ) | 13–30 |
| Gamma ( $\gamma$ ) | > 30 |

**Table 2.**
*Frequency waves of the human brain rhythms.*

categorization of the vigilance states of comatose patients, based on their EEG data, has been explored and yielded intriguing findings, which will be discussed in Section 3.3. Additionally, the differentiation between alcohol consumption and nonconsumption has been achieved through the analysis of EEG-recorded signals. The potential effectiveness of this approach will be further examined in Section 4.1. Furthermore, EEGs have been employed in the ICU to enhance patient comfort, identify brain death, and evaluate recovery. These topics will be elaborated upon in the subsequent sections.

Typically, researchers follow a series of steps to apply computational methods to EEG data to classify or detect diseases or abnormal activities. The initial step involves cleaning the data to remove artifacts and interference. Subsequently, they employ specific methods tailored to the task at hand. In the realm of ICU and other EEG-related fields, feature extraction is a commonly used technique in computer applications. As such, we are dedicating this section of the introduction to discuss various brain waves. **Table 2** indicates the traditional wave bands of the human brain, often referred to as brain rhythms. It is noteworthy that the gamma band can occasionally reach up to 200 Hz, although it typically ranges between 30 and 100 Hz [14].

In general, each of the rhythms is seen for specific states of the subject. The delta band appears in a deep sleep state, while theta appears during drowsiness or meditation; the alpha band appears during a relaxed but awake state, and the beta band appears during a focused or alert state of consciousness, while the gamma band appears when the subject is in an attentive or learning state [15].

## 2. Problems of EEG recording in the ICU

It has been more than 80 years since electroencephalography was first used in comatose patients, but it still faces some challenges to this day. Fortunately, these problems have been largely overcome due to the diligent efforts of researchers. Mobile EEG headsets have reduced the risks associated with moving comatose patients to stationary EEG machines. This transfer previously required numerous mobile ICU equipment and personnel. With the advent of mobile EEG headsets, recording data from comatose patients has become much simpler and typically requires only one person. Unfortunately, not all ICUs are equipped with these mobile EEG headsets, which are increasingly becoming a necessity to reduce risks and improve patient comfort.

Due to electrode sensitivity to outlier signals and different sedative drug effects on electrical brain activities, the recorded EEG data in the ICU are mainly affected by two major problems: (1) artifacts and interference and (2) the sedation effects.

### 2.1 The dilemma of artifacts and interference

Artifacts are one of the biggest problems of EEG recordings. The presence of artifacts on the EEG recordings of an ICU patient is higher than in any other medical department.

As shown in **Figure 1**, the ICU room is occupied by many electrical machines that could affect the electroencephalogram of the comatose patients; additionally, line noise and room ventilation could be part of the artifact present in the recordings. Medical examination and nursing care if being close to the head of the patient showed high-amplitude interference during our recording. The environmental signals are not the only signals that could affect the data; the physiological non-brain electrical signals are the major source of artifacts in EEG recordings. **Table 3** presents the general causes of artifacts and interference during an EEG recording in the ICU.

To obtain clean data that could be useful for further human or computer analysis, researchers invented several techniques. In this paragraph, we mention the most successful ones: The independent component analysis (ICA) is the most popular method used to recover brain signals from recorded EEG signals. It is a blind source separation (BSS) technique based on the assumption that the mixture of the recorded signals donated by $X(t)$ is related to the source signals $S(t)$ as follows:

$$X(t) = W^{*}S(t) \tag{1}$$

where $W$ is a mixing matrix [16]. The canonical correlation analysis (CCA) is also a BSS-based technique that uses second-order statistics, which makes it have a shorter computational time compared to ICA, which uses higher-order statistics. It separates the components from uncorrelated sources [17]. The empirical mode decomposition (EMD) was proposed by Huang et al. for the analysis of the nonstationary signal in 1998 [18]. It is a single-channel decomposition method. Its algorithm decomposes the mixed signal $X(t)$ into a set of components based on an amplitude-frequency modulation [18, 19]. The artifact removal techniques discussed earlier have demonstrated

**Figure 1.**
*A comatose patient in an ICU room during EEG recordings using a mobile headset.*

| Physiological | Environmental |
|---|---|
| Electromyography (EMG) | Line noise |
| Electrooculography (EOG) | Electrodes malfunctions |
| Electrocardiography (ECG) | Electrical machines |
| Deep breathing | Medical and nursing care |

**Table 3.**
*Physiological and environmental causes of artifacts and interference.*

significant effectiveness in isolating artifacts from EEG data, whether applied individually or in combination. In our previous work [20], we employed a variety of methods to eliminate both artifacts and interference.

### 2.2 Effects of sedative drugs on the EEG

Sedation plays a vital role in numerous patient scenarios. Its primary purposes include pain relief, managing patient restlessness, reducing anxiety, and helping in treatment procedures. The sedatives employed exert a variety of influences on the brain's electrical activity. These altered patterns correlate with the cognitive state and memory of the individuals. The extent of these effects fluctuates based on the dosage of the sedative drugs, which regulate the patient's level of anesthesia, ranging from conscious and moderate to deep sedation.

The initial surveillance of anesthetized states using electroencephalography (EEG) was pioneered in the 1950s [21, 22]. Since this groundbreaking work, the impact of sedative drugs on EEG readings has been recognized, prompting researchers to delve into the effects of various sedatives, such as midazolam [23] and propofol [24], on brain activity. Veselis compiled the influences of these sedatives at different concentrations [25]. The primary alterations observed are changes in the rhythms of wave bands and power spectrum, either in specific brain areas or across the entire cerebral cortex.

In [26], Spencer et al. employed spectral analysis to quantify the level of anesthesia in ICU patients. The study by Shearer [27] demonstrated a strong correlation between the depth of sedation and the EEG patterns. Researchers in [28] compared the impacts of dexmedetomidine and propofol on EEG patterns (varying wave power) across different brain regions during moderate and deep sedation, in conjunction with the Observer's Assessment of Alertness and Sedation (OAA/S) score. The concurrent use of such scores with EEG has been shown to enhance the efficiency of research work. In this section, we present a comprehensive overview of the challenges associated with EEG recordings in the ICU. We also introduced proposed strategies for artifact removal and patient transfer, which are grounded on research findings. The potential solutions to mitigate the effects of sedative drugs on EEG recordings will be explored in Section 4.

## 3. Promising new findings

In the introduction, we highlighted the significance of EEG in the intensive care unit, particularly its role in diagnosing and monitoring the progress of comatose patients. In this section, we will delve into some of the latest discoveries stemming from computer analysis of EEG data. These findings could potentially revolutionize the care of comatose patients, enhancing their well-being and providing a deeper understanding of their condition.

### 3.1 Bad sleep quality effects on comatose patients

Quality sleep is crucial for everyone, including comatose patients. These patients may experience sleep deprivation due to various factors, which could potentially exacerbate their condition. Palesh et al. [29] found a high link between poor night sleep and pain intensity during the day. On the other side, experiencing sleep deprivation can be a reason for extreme sensitivity to pain [30]. Kamdar et al. [31] found that approximately 80% of ICU patients experience sleep deprivation during their hospital stay. Normal sleep is composed of 4–5 of the following cycle N1 $\rightarrow$ N2 $\rightarrow$ N3 $\rightarrow$ REM sleep in adults. Kamdar et al. [32] found that the architecture of sleep in ICU patients is quite abnormal, where the majority of sleep time is spent in stages N1 and N2 with little or no time spent at stage N3 and REM sleep while these two stages are critical for physical healing and growth and emotional healing, and brain restoration, respectively, as found by Evan [33]. Jones et al. [34] showed that psychological outcomes such as anxiety, depression, and post-traumatic stress disorder (PTSD) could follow the experience of severe pain in the ICU. Sessler [35] found that sleep deprivation associated with the ICU environment could worsen the patient's pain experience. The manor or major undergoes procedures that are often performed by nurses or doctors; some of them are painful, and some others are particularly stressful; this can be the result of sleep disorder [36].

The literature and references previously mentioned categorize the causes of sleep deprivation into environmental and bio-cognitive causes. The most common environmental causes in the ICU are noise and light. Salas and Gamaldo found that light is more responsible for awakening than noise in the ICU, followed by temperature and bed discomfort [30].

Sleep deprivation poses a significant challenge in the recovery of comatose patients. In many cases, ICU staff struggle to identify whether a patient is suffering from sleep deprivation, especially those with a low level of consciousness. This is due to the lack of reliability of the sleep scores. Over the past few decades, researchers have begun to use EEG to investigate sleep quality. Mohammadi et al. [37] presented a classification of sleep stages based on the singularity spectrum analysis of EEG signals. They achieved a 71% accuracy rate using a support vector machine (SVM) to classify features of a single EEG channel C3-A2. To enhance the classification of different sleep stages, Shi et al. [38] extracted features from multiple EEG channels and classified them based on a machine learning approach, achieving a 10% increase in accuracy. Pain is a significant bio-cognitive factor that contributes to sleep deprivation in the ICU. Both sleep deprivation and pain are closely associated with stress. The latter will be explored in the subsequent section, while pain assessment will be discussed in Section 4.

### 3.2 Investigation of stress in the ICU

Celik et al. [39] concluded "Patients in an ICU environment are often subjected to heightened levels of stress and anxiety due to factors such as immobility, sedation, and the performance of intimate and invasive procedures by unfamiliar individuals." Selye [40] enumerates several causes of stress in human life. Among these, those that can be associated with the stress experienced by ICU patients include surgical trauma, emotional arousal, fatigue, pain, fear, frustration, and drug intoxication. Additionally, factors specific to the ICU environment, such as discomfort, being surrounded by strangers, and the absence of family members, can also contribute to the stress experienced by these patients.

During a stressed state, changes occur in the mental condition that can affect the electrical activity of the brain; thus, EEG can be a tool to detect these cognitive changes. Therefore, in detecting human stress, EEG has become a highly used technique over the last couple of decades. Several papers classified stress levels based on the human brain's electrical signals. For example, in [41, 42], the authors proved that the similarity between the stressed state and the negative emotions states obtains 90% accuracy for the classification of stressed and stress-free groups by extracting features from Higuchi's fractal dimension, Gaussian mixtures, and magnitude square coherence estimation (MSCE). In [42, 43] the authors found that the levels of stress are correlated with the power spectrum features of frequency ranges of the $\theta$, $\lambda$, and $\alpha$ bands. The identification of the existence of stress is based on changes in the EEG alpha and theta band since (1) the $\alpha$ band is dominant when the brain is in a relaxation mode (no activity) and (2) in the case of a stress state, the power of the $\alpha$ wave will decrease, while the $\theta$ waves increase. Paraschiv et al. [44] observed higher levels of beta activity in participants diagnosed as stressed. In [45, 46], it is reported that the increase in EEG amplitude at the frequencies of 19–22 Hz and high beta 35 Hz is specific to stress. Adochiei et al. [47] concluded that chronic stress has been associated with high levels of beta power. The papers mentioned above classified stress levels based on the human brain's electrical signals.

In [48], multilayer perception (MPL) plus SVM classifier have been employed to distinguish between different stress levels where the headset used is an EMOTIV EPOC +. Hou et al. [43] presented a 4 stress levels (relaxed, engrossed, stressful, and anxious) identification algorithm combining fractal dimension and statistical features where the classifier is a support vector machine (SVM). In [49], an EMOTIV EPOC wireless device uses the relative difference between beta and alpha power as features to identify the level of stress.

### 3.3 EEG for comatose patients vigilance state classification

Recently, we have conducted a study, the findings of which are illustrated in **Figure 2** and showing that the classification of patient vigilance states is possible based on their EEG signals. In that paper, we discussed the possibility of overcoming physiological and behavioral coma scale scores, especially due to the number of limitations of the coma scales. We demonstrated that the singularity spectrum of a single-channel EEG can be utilized as an effective tool to classify the vigilance state of comatose patients. The study in question, with its results exhibited in **Figure 2**, was carried out in three different groups of patients with Glasgow Coma Scale scores of 3, 7, and sedated. Based on these findings, the multifractal analysis of EEG data could be a tool to determine the level of consciousness of patients in a coma, which could overcome the limited physiological and behavioral coma scales.

### 3.4 EEG for brain death diagnosis

A brain death is the complete and permanent loss of function of the entire brain and the brain stem. One of the four criteria for declaring brain death according to the

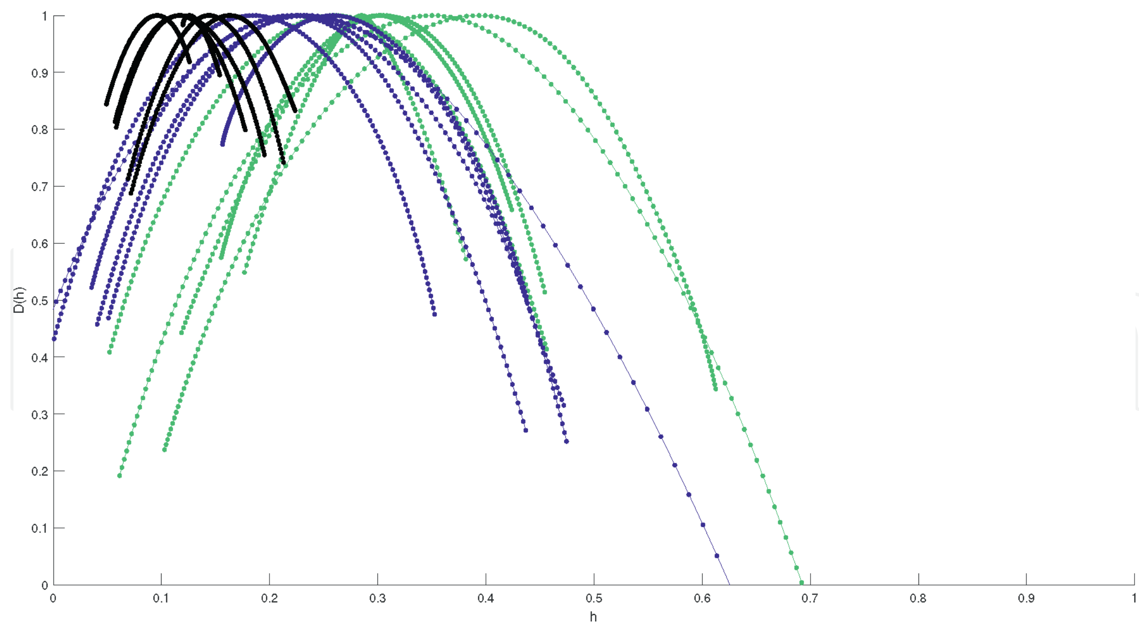


**Figure 2.**
*Singularity spectrum curves of 3 groups of comatose patients: black color for sedated patients, blue color for patients with GCS = 3, and green color for patients with GCS = 7.*

Harvard Medical School committee is a flat EEG [50]. In simpler terms, the diagnosis of brain death is typically based on specific criteria and follows a detailed process. This process can be time-consuming and carries certain risks, such as the need to disconnect the ventilator during the apnea test. EEG recordings are easily accessible and safe. EEG readings can sometimes be distorted by various forms of interference or artifacts discussed in Section 2.1, leading to an underestimation of their true value. Despite these challenges, there is no denying that a thorough and numerical analysis of EEG data can provide invaluable insights in the fields of neurology and clinical medicine [51]. In simpler terms, a positive result from an EEG test indicates that the brain is working. As a result, a patient in a deep coma may still exhibit some electrical activity in the brain, as detected by the EEG. However, a brain-dead patient will not show such activity. Even with the variation of criteria over time or from one country to another, EEG is the most frequently required test. It is mandatory in 28% and optional in 47% of countries [52]. Electrocerebral inactivity (ECI) was defined as "the absence over all regions of the head of identifiable electrical activity or cerebral origin, whether spontaneous or induced by physiologic stimuli and pharmacological" by the glossary of the International Federation of Clinical Neurophysiology [53]. Compared to the apnea test, EEG is less risky for brain death analysis. Researchers in [54, 55] proposed a CCA approach to distinguish brain death and deep coma based on patients' EEG signals. They concluded that the relative power spectrum density in the delta wave and the permutation entropy can be effectively considered as potential distinguishing characteristics when analyzing the differences between patients in a coma and those who are brain-dead.

### 3.5 EEG for prognosticate recovery in comatose patients

EEG is one of a number of neuroprognostic tools that are used to diagnose ischemic brain injury and predict recovery. Bouchereau et al. [56] proposed a quantitative EEG marker based on brain wave classification to predict awakening and recovery of consciousness in patients with severe brain injury. The automatic detection and assessment of comatose patients' recovery represent a compelling area of research. Further investigation by researchers is crucial to unlock its full potential.

EEG has also been used to investigate and identify depression biomarkers [57] and many other applications for the comfort of comatose patients.

## 4. Possible new applications

In this section, we would like to shed some light on a few EEG applications that have been used outside the ICU and showed reliable results. Thus, these applications could be investigated in comatose patients and could overcome many limitations that affect the good understanding of the medical staff of the condition of a comatose patient.

### 4.1 Alcohol detection and classification

As previously mentioned, the consumption of alcohol a few hours before ICU admission can significantly impact the reliability of many coma scales due to its effect on brain function responses. Long-term alcohol use can lead to a significant loss of neuronal connections.

Much research has investigated the possibility of a classification of EEG signals from alcoholic patients using a variety of methods. For example, Aprilla et al. [57] used a texture analysis method known as GLDM to extract features from 64 channels and classify alcoholic and nonalcoholic EEG signals. However, the accuracy of this method did not exceed 70%. Fattah et al. [58] utilized feature extraction from EEG signals to classify the EEG signals of alcoholic and nonalcoholic subjects, achieving an accuracy of 95%. Then, Mumtaz et al. [59] employed spectral entropy for specific sub-bands of EEG signals to detect event-related potential related to alcohol consumption. Wavelet decomposition has also been used for feature extraction from EEG signals for the detection and classification of alcoholic EEG signals [60]. It is noteworthy that most studies investigating alcohol consumption using EEG recording have focused on the Gamma sub-band [61, 62].

These methods have been implemented on conscious subjects during visually related events. However, only a small number of these methods have achieved an accuracy rate exceeding 90%, indicating that there is substantial room for improvement in this approach. Despite this, the potential for detecting alcohol-related EEG patterns is promising. This could be particularly beneficial in the ICU, especially upon admission. The ability to determine whether a comatose patient has consumed alcohol or not before accidents or any other cause of loss of consciousness could significantly enhance our understanding of the patient's condition.

### 4.2 EEG-based pain severity detection

The use of EEG to investigate pain in humans has emerged in the last decade. For instance, Van Der Miesen et al. [63] and Mouraux and Iannetti [64] found that the primary somatosensory cortex (S1), the anterior cingulate cortex (ACC), and the insular cortex brain regions are the regions involved in processing affective and sensory acute pain. In addition, Sun et al. [65] used the regions mentioned above in addition to the precentral gyrus (M1) to detect acute pain using an EEG headset. To enhance pain assessment in comatose individuals, further investigation is warranted. Large-scale studies using diverse techniques and refined by automatic detection algorithms are essential. Achieving this would enable accurate pain assessment in comatose patients, leading to more targeted and effective treatments. Ultimately, this approach could reduce reliance on painkiller drugs.

### 4.3 EEG-based coma and sedation scales

The utilization of multifractal analysis in EEG signal processing has demonstrated significant advances in classification. The findings discussed in Section 3.3 have the potential to be expanded to a coma scale scoring system, which would be based on the extraction of multifractal properties from EEG signals. Further investigation of this approach could lead to the development of an innovative scoring system to assess the coma scale of patients in ICUs. Moreover, the characterization of EEG signals from sedated patients (represented by the black curves) is feasible due to the distinct length of their shape compared to the singularity spectrum curves of non-sedated patients. This aspect forms a key area of focus in our upcoming project work. By developing a coma scale grounded in the analysis of electrical brain signals from comatose patients, we can transcend the limitations of existing scoring systems that are dependent exclusively on physiological and behavioral responses.

## 5. Conclusion

EEG has recently been utilized to delve into several coma-related aspects, such as sleep quality analysis, pain evaluation, sedation monitoring, and stress assessment. Although the findings of these studies are varied and await validation, they exhibit encouraging potential. These insights could pave the way for a novel approach to understanding the needs of comatose patients. In the previous couple of sections, we highlighted the strong correlation between pain, stress, and sleep deprivation in comatose patients, emphasizing that the presence of one could exacerbate the others. With the advent of new findings from EEG-based investigations related to coma, it has become possible to detect and assess these three factors. Early detection could potentially speed up patient recovery. Furthermore, EEG data could be leveraged to overcome the limitations of the currently used scales, thereby improving our understanding of the condition of comatose patients. Although most of the findings discussed require validation and application in larger samples, they represent the challenges faced by ICU department doctors. These challenges, when addressed, could improve the well-being of comatose patients and improve our understanding of coma.

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## References

[1] Berger H. Uber das Elektrenkephalogramm des menschen; Funfte Mitteilung. Archiv fur Psychiatrie und Nervenkrankheiten. 1932;**98**:231-254

[2] Penfield W, Rasmussen T. The Cerebral Cortex of Man; A Clinical Study of Localization of Function. APA PsyNet; 1950

[3] Wunsch K, Wurst R, von Dawans B, Strahler J, Kasten N, Fuchs R. Habitual and acute exercise effects on salivary biomarkers in response to psychosocial stress. Psychoneuroendocrinology. 2019;**106**:216-225

[4] Bienertova-Vasku J, Lenart P, Scheringer M. Eustress and distress: Neither good nor bad, but rather the same? BioEssays. 2020;**42**(7):1900238

[5] Katmah R, Al-Shargie F, Tariq U, Babiloni F, Al-Mughairbi F, Al-Nashash H. A review on mental stress assessment methods using EEG signals. Sensors. 2021;**21**(15):5043

[6] Chu B, Marwaha K, Sanvictores T, Ayers D. Physiology, stress reaction. In: StatPearls [Internet]. StatPearls Publishing; 12 Sep 2022

[7] Can YS, Arnrich B, Ersoy C. Stress detection in daily life scenarios using smart phones and wearable sensors: A survey. Journal of Biomedical Informatics. 2019;**92**:103139

[8] Grosso M, Domingos R, Serápio F, Alves K, Castro C. Most used pain assessment scales in the unconscious critical patient: A systematic review. Annals of Medicine. 2019;**51**(sup1):208

[9] Staffe AT, Bech MW, Clemmensen SL, Nielsen HT, Larsen DB, Petersen KK. Total sleep deprivation increases pain sensitivity, impairs conditioned pain modulation and facilitates temporal summation of pain in healthy participants. PLoS One. 2019;**14**(12):e0225849

[10] Klinzing JG, Niethard N, Born J. Mechanisms of systems memory consolidation during sleep. Nature Neuroscience. 2019;**22**(10):1598-1610

[11] Dorsch JJ, Martin JL, Malhotra A, Owens RL, Kamdar BB. Sleep in the intensive care unit: Strategies for improvement. Seminars in Respiratory and Critical Care Medicine. 2019;**40**(05):614-628

[12] Lewandowska K, Medrzycka-Dabrowska W, Kwiecień-Jaguś K, Czyż-Szypenbejl K. Factors determining sleep in patients hospitalised in ICUs in a hospital in northern Poland. Sleep and Biological Rhythms. 2019;**17**:243-250

[13] Reith FC, Van den Brande R, Synnot A, Gruen R, Maas AI. The reliability of the Glasgow coma scale: A systematic review. Intensive Care Medicine. 2016;**42**:3-15

[14] Jones SR. When brain rhythms aren't 'rhythmic': Implication for their mechanisms and meaning. Current Opinion in Neurobiology. 2016;**40**:72-80

[15] Aboalayon KA, Ocbagabir HT, Faezipour M. Efficient sleep stage classification based on EEG signals. In: IEEE Long Island Systems, Applications and Technology (LISAT) Conference 2014. IEEE; 2 May 2014. pp. 1-6

[16] Islam MK, Rastegarnia A, Yang Z. Methods for artifact detection and

removal from scalp EEG: A review. Neurophysiologie Clinique/Clinical Neurophysiology. 2016;**46**(4-5):287-305

[17] Borga M, Friman O, Lundberg P, Knutsson H. A canonical correlation approach to exploratory data analysis in fMRI. In: ISMRM 10th Scientific Meeting & Exhibition, 18-24 May 2002, Honolulu, Hawai'i, USA. 2002

[18] Huang NE, Shen Z, Long SR, Wu MC, Shih HH, Zheng Q, et al. The empirical mode decomposition and the Hilbert spectrum for nonlinear and non-stationary time series analysis. Proceedings of the Royal Society of London. Series A: Mathematical, Physical and Engineering Sciences. 1998;**454**(1971):903-995

[19] Chavez M, Grosselin F, Bussalb A, Fallani FD, Navarro-Sune X. Surrogate-based artifact removal from single-channel EEG. IEEE Transactions on Neural Systems and Rehabilitation Engineering. 2018;**26**(3):540-550

[20] Hbibi B, Khiari C, Wirsing K, Mili L, Baccar K, Mami A. Identifying and removing interference and artifacts in multifractal signals with application to EEG signals. IEEE Access. 2023;**11**:119090-119105. DOI: 10.1109/ACCESS.2023.3325786

[21] Mayo CW, Bickford RG, Faulconer A. Electroencephalographically controlled anesthesia in abdominal surgery. Journal of the American Medical Association. 1950;**144**(13):1081-1083

[22] Verzeano M. Servo-motor integration of the electrical activity of the brain and its applications to the automatic control of narcosis. Electroencephalography and Clinical Neurophysiology. 1951;**3**(1):25-30

[23] Merlo F, Lion P. Study of the rapid EEG activity induced by midazolam. Current Therapeutic Research. 1985;**38**(5):798-807

[24] Seifert HA, Blouin RT, Conard PF, Gross JB. Sedative doses of propofol increase beta activity of the processed electroencephalogram. Anesthesia & Analgesia. 1993;**76**(5):976-978

[25] Veselis RA. The EEG as a monitor of sedation: Encouraging progress. Journal of Clinical Anesthesia. 1996;**8**(3):S81-S87

[26] Spencer EM, Green JL, Willatts SM. Continuous monitoring of depth of sedation by EEG spectral analysis in patients requiring mechanical ventilation. BJA: British Journal of Anaesthesia. 1994;**73**(5):649-654

[27] Shearer CB. An Investigation into the Validity, Reliability and Clinical Utility of the Hillside Assessment of Perceived Intelligences. The Union Institute; 1991

[28] Xi C, Sun S, Pan C, Ji F, Cui X, Li T. Different effects of propofol and dexmedetomidine sedation on electroencephalogram patterns: Wakefulness, moderate sedation, deep sedation and recovery. PLoS One. 2018;**13**(6):e0199120

[29] Palesh OG, Collie K, Batiuchok D, Tilston J, Koopman C, Perlis ML, et al. A longitudinal study of depression, pain, and stress as predictors of sleep disturbance among women with metastatic breast cancer. Biological Psychology. 2007;**75**(1):37-44

[30] Salas RE, Gamaldo CE. Adverse effects of sleep deprivation in the ICU. Critical Care Clinics. 2008;**24**(3):461-476

[31] Kamdar BB, Needham DM, Collop NA. Sleep deprivation in critical illness: Its role in physical and psychological recovery. Journal of Intensive Care Medicine. 2012;**27**(2):97-111

[32] Tranmer JE, Minard J, Fox LA, Rebelo L. The sleep experience of medical and surgical patients. Clinical Nursing Research. 2003;**12**(2):159-173

[33] Evans BM. Sleep, consciousness and the spontaneous and evoked electrical activity of the brain. Is there a cortical integrating mechanism? Neurophysiologie Clinique/Clinical Neurophysiology. 2003;**33**(1):1-0

[34] Jones C, Bäckman C, Capuzzo M, Flaatten H, Rylander C, Griffiths RD. Precipitants of post-traumatic stress disorder following intensive care: A hypothesis generating study of diversity in care. Intensive Care Medicine. 2007;**33**:978-985

[35] Sessler CN. Progress toward eliminating inadequately managed pain in the ICU through interdisciplinary care. Chest. 2009;**135**(4):894-896

[36] Pudas-Tähkä SM, Axelin A, Aantaa R, Lund V, Salanterä S. Pain assessment tools for unconscious or sedated intensive care patients: A systematic review. Journal of Advanced Nursing. 2009;**65**(5):946-956

[37] Mohammadi SM, Kouchaki S, Ghavami M, Sanei S. Improving time–frequency domain sleep EEG classification via singular spectrum analysis. Journal of Neuroscience Methods. 2016;**273**:96-106

[38] Shi J, Liu X, Li Y, Zhang Q, Li Y, Ying S. Multi-channel EEG-based sleep stage classification with joint collaborative representation and multiple kernel learning. Journal of Neuroscience Methods. 2015;**254**:94-101

[39] Celik S, Öztekin D, Akyolcu N, İşsever H. Sleep disturbance: The patient care activities applied at the night shift in the intensive care unit. Journal of Clinical Nursing. 2005;**14**(1):102-106

[40] Selye H. Stress in Health and Disease. Butterworth-Heinemann; 2013

[41] Seo SH, Lee JT, Crisan M. Stress and EEG. In: Convergence and Hybrid Information Technologies. Croatia: InTech; 1 Mar 2010. p. 27

[42] Khosrowabadi R, Quek C, Ang KK, Tung SW, Heijnen M. A brain-computer interface for classifying EEG correlates of chronic mental stress. In: The 2011 International Joint Conference on Neural Networks, San Jose, CA, USA. 2011. pp. 757-762. DOI: 10.1109/IJCNN.2011.6033297

[43] Hou X, Liu Y, Sourina O, Tan YRE, Wang L, Mueller-Wittig W. EEG based stress monitoring. In: 2015 IEEE International Conference on Systems, Man, and Cybernetics, Hong Kong, China. 2015. pp. 3110-3115. DOI: 10.1109/SMC.2015.540

[44] Paraschiv R, Bănică CK, Adochiei IR, Dorobantu LE, Cotorobai DM, Manea I. Comparative study of stress using the classical method and EEG wave processing. In: 2022 E-Health and Bioengineering Conference (EHB), Iasi, Romania. 2022. pp. 01-04. DOI: 10.1109/EHB55594.2022.9991607

[45] Gupta S, Deep K, Mirjalili S, Kim JH. A modified sine cosine algorithm with novel transition parameter and mutation operator for global optimization. Expert Systems with Applications. 2020;**154**:113395

[46] Cepisca, Adochiei FC, Potlog S, Banica CK, Seritan GC. Platform for bio-monitoring of vital parameters in critical infrastructures operation. In: 2015 7th International Conference on Electronics, Computers and Artificial Intelligence (ECAI), Bucharest, Romania. 2015. p. E-7-E-10. DOI: 10.1109/ECAI.2015.7301144

[47] Adochiei F-C et al. Brain mapping using a Blockchain approach. In: 2019 E-Health and Bioengineering Conference (EHB), Iasi, Romania. 2019. pp. 1-4. DOI: 10.1109/EHB47216.2019.8970089

[48] Kamińska D, Smółka K, Zwoliński G. Detection of mental stress through EEG signal in virtual reality environment. Electronics. 2021;**10**(22):2840

[49] Jun G, Smitha KG. EEG based stress level identification. In: 2016 IEEE International Conference on Systems, Man, and Cybernetics (SMC), Budapest, Hungary. 2016. pp. 003270-003274. DOI: 10.1109/SMC.2016.7844738

[50] Allen N, Burkholder J, Comiscioni J. Clinical criteria of brain death. Annals of the New York Academy of Sciences. 1978;**315**(1):70-96

[51] Chen Z, Cao J, Cao Y, Zhang Y, Gu F, Zhu G, et al. An empirical EEG analysis in brain death diagnosis for adults. Cognitive Neurodynamics. 2008;**2**:257-271

[52] Wahlster S, Wijdicks EF, Patel PV, Greer DM, Hemphill JC III, Carone M, et al. Brain death declaration: Practices and perceptions worldwide. Neurology. 2015;**84**(18):1870-1879

[53] Stecker MM, Sabau D, Sullivan L, Das RR, Selioutski O, Drislane FW, et al. American clinical neurophysiology society guideline 6: Minimum technical standards for EEG recording in suspected cerebral death. Journal of Clinical Neurophysiology. 2016;**33**(4):324-327

[54] Zhu L, Cui G, Cao J, Cichocki A, Zhang J, Zhou C. A hybrid system for distinguishing between brain death and coma using diverse EEG features. Sensors. 2019;**19**(6):1342

[55] Lambeck J, Strecker C, Niesen WD, Bardutzky J. Exclusive color-coded duplex sonography of extracranial vessels reliably confirms brain death: A prospective study. Frontiers in Neurology. 2022;**13**:992511

[56] Bouchereau E, Marchi A, Hermann B, Pruvost-Robieux E, Guinard E, Legouy C, et al. Quantitative analysis of early-stage EEG reactivity predicts awakening and recovery of consciousness in patients with severe brain injury. British Journal of Anaesthesia. 2023;**130**(2):e225-e232

[57] Aprillia BS, Rizal A, Fauzi MA. Grey level differences matrix for alcoholic EEG signal classification. JOIV: International Journal on Informatics Visualization. 2024;**8**(1):26-30

[58] Fattah SA, Fatima K, Shahnaz C. An approach for classifying alcoholic and non-alcoholic persons based on time domain features extracted from EEG signals. In: 2015 IEEE International WIE Conference on Electrical and Computer Engineering (WIECON-ECE), Dhaka, Bangladesh. 2015. pp. 479-482. DOI: 10.1109/WIECON-ECE.2015.7443972

[59] Mumtaz W, Vuong PL, Malik AS, Rashid RB. A review on EEG-based methods for screening and diagnosing alcohol use disorder. Cognitive Neurodynamics. 2018;**12**:141-156

[60] Dewi Purnamasari P, Ratna AAP, Kusumoputro B. Relative wavelet bispectrum feature for alcoholic EEG signal classification using artificial neural network. In: 2017 15th International Conference on Quality in Research (QiR): International Symposium on Electrical and Computer Engineering, Nusa Dua, Bali, Indonesia. 2017. pp. 154-158. DOI: 10.1109/QIR.2017.8168473

[61] Palaniappan R. Screening for chronic alcoholic subjects using multiple gamma band EEG: A pilot study. Journal of

Computer Science and Technology. 2007;**7**(02):182-185

[62] Widadi R, Soesanti I, Wahyunggoro O. EEG classification using elliptic filter and multilayer perceptron based on gamma activity features. In: 2018 4th International Conference on Science and Technology (ICST), Yogyakarta, Indonesia. 2018. pp. 1-5. DOI: 10.1109/ICSTC.2018.8528568

[63] Van Der Miesen MM, Lindquist MA, Wager TD. Neuroimaging-based biomarkers for pain: State of the field and current directions. Pain Reports. 2019;**4**(4):e751

[64] Mouraux A, Iannetti GD. The search for pain biomarkers in the human brain. Brain. 2018;**141**(12):3290-3307

[65] Sun G, Wen Z, Ok D, Doan L, Wang J, Chen ZS. Detecting acute pain signals from human EEG. Journal of Neuroscience Methods. 2021;**347**:108964