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Sleep analysis in a CLIS patient using soft-clustering: a case study

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Abstract. The paper deals with the analysis of the sleep patterns of a patient with Completely Locked-In Syndrome (CLIS). The analysis was performed using an approach initially designed to detect consciousness in Disorders of Consciousness (DoC) and CLIS patients. The method extracts different features based on spectral, complexity and connectivity measures and performs soft-clustering analyses to determine the consciousness state. The results showed that it was able to discriminate between the (Non)-Rapid Eye Movement (NREM) and the Rapid Eye Movement (REM) sleep stages. Detecting normal Slow-Wave Sleep (SWS) and REM phases indicates better communication abilities for the patient.

1 Introduction

Completely Locked-In Syndrome (CLIS) is a condition in which a person is conscious but is unable to perform any muscle movements such as walking and talking [1]. Due to the rarity of the condition as well as the limited access to patients' data, only a handful of studies have been done to analyse such patients' sleep patterns. In healthy subjects, there are five stages of sleep that can be grouped into two categories: Non-Rapid Eye Movement (NREM) or deep sleep and Rapid Eye Movement (REM) sleep [2]. The latter is usually associated with dreaming and irregular muscle movements in addition to rapid movements of the eyes, which makes it difficult to determine in CLIS patients [3]. REM is also characterised by a highly active brain with brainwaves similar to those during wakefulness, and is considered a secondary conscious state [2, 4]. Secondary consciousness is a subjective awareness that involves perception and emotion enhanced by thinking and the awareness of being aware [4].

In this paper, an approach originally designed to assess consciousness in patients with disorders of consciousness (DoC) [5] and CLIS [6] is adapted and used to detect REM sleep stages in one CLIS patient. Various features are extracted from the EEG signal. They consist of spectral features such as the relative powers in the θ and β bands and the spectral edge frequency (SEF), complexity features (Poincaré plots and Lempel-Ziv complexity (LZC)), and connectivity features consisting of the imaginary part of the coherency (iCOH) and the weighted symbolic mutual information (wSMI).

The patient and data used for the analysis is presented in Section 2, followed by brief description of the features used and the machine learning algorithms used. The results are presented in Section 3, followed by a discussion before concluding in Section 4.

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2 Tools and Methods

2.1 Data acquisition and pre-processing

The sleep data was recorded from an 80 years old female CLIS patient that was diagnosed with ALS in 2010 [7]. The data was recorded for two consecutive nights, however only the second night was used for the analysis. The first night was used to familiarise the patient with the electrodes [3]. In addition to the EEG, EMG and EOG were also recorded, although only the former were used in this study. The EEG data consisted of recordings from 6 channels located in the frontal, central, and occipital areas of the brain: F3, F4, C3, C4, O1 and O2. according to the 10-20 system [8]. The electrodes were referenced to a channel on the right mastoid, and the middle frontal electrode Fz was used as ground. The sampling frequency is 500 Hz. The raw EEG data was filtered between 0.1 and 30 Hz using a third order Butterworth bandpass filter, and subsequently segmented into 30-s segments as usual for sleep analysis [3].

2.2 Features computation

All analysis were performed with MATLAB R2023a. The approach used in this study was originally designed to assess CLIS patients' consciousness [7, 6, 5] and adapted here for sleep analysis. Several features comprising spectral, complexity and connectivity measures were therefore extracted from the pre-processed EEG signals.

Brain recordings oscillate at different frequencies and provide information about the brain states [9]. The spectral features consisted of the relative powers (RP) [10] in the θ (4 - 8 Hz) and β (12 - 30 Hz) bands, computed using Eq. 1 for a signal $x(t)$.

$$RP = \frac{\sum_{f=f_1}^{f_2} S_x(f)}{\sum_{f=0}^{30} S_x(f)}, \tag{1}$$

where S_x is the power spectral density of the signal $x(t)$, $f1$ (resp. $f2$) is the lower (resp. upper) limit of the frequency band of interest.

In addition, the frequency below which 95% of the EEG power are located, called Spectral Edge Frequency (SEF95) [11], was also calculated using Eq. 2.

$$\sum_{f=0}^{SEF95} S_x(f) = 0.95 \sum_{f=0}^{Fs/2} S_x(f). \tag{2}$$

where Fs is the sampling frequency.

The randomness of a signal are determined by its complexity. To that intent, Poincaré plots determine it geometrically by plotting them against their delayed with a lag τ version [12]. The signal complexity is then determined by the Ellipsoid Radius Ratio (ERR), which is the ratio $SD1/SD2$ (Eq. 3) [13]. SD2 and SD1 are respectively the standard deviation of the points along and perpendicular to the line of identity on the Poincaré plots.

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$$ERR = \frac{SD1}{SD2} = \frac{\frac{\sqrt{2}}{2} SD(x(t) - x(t+\tau))}{\sqrt{2SD(x(t))^2 - \frac{1}{2} SD(x(t) - x(t+\tau))^2}} \tag{3}$$

On the other hand, LZC uses a more analytical approach that employs a symbolic representation of the signal to determine its complexity [14]. Both complexity measures are calculated using Eq. 4 and 5, respectively.

$$x_a(t) = x(t) + i x_h(t) \tag{4}$$

$$S(t) = \begin{cases} 0, & \text{if } abs\left(x_h(t)\right) \leq mean\left(abs\left(x_h(t)\right)\right) \\ 1, & \text{otherwise} \end{cases} \tag{5}$$

where $x_a(t)$ is the analytic signal related to $x(t)$, and $x_h(t)$ is the Hilbert transform of $x(t)$ [15].

Brain connectivity provides information on the connections between different brain regions. Linear relationships between the different pairs of channels were determined using iCOH [16] using Eq. 6. Linear and non-linear relations between them were computed using the wSMI [17, 18] in Eq. 7.

$$iCOH_{xy}(f) = \Im\left(\frac{S_{xy}(f)}{\sqrt{S_{xx}(f) \cdot S_{yy}(f)}}\right) \tag{6}$$

where $S_{xy}(f)$ is the cross power spectral density of the signals $x(t)$ and $y(t)$.

$$wSMI(x,y) = \frac{1}{\log(k!)} \sum_{\hat{x} \in \hat{X}} \sum_{\hat{y} \in \hat{Y}} w(\hat{x},\hat{y}) p(\hat{x},\hat{y}) \log\left(\frac{p(\hat{x},\hat{y})}{p(\hat{x})p(\hat{y})}\right) \tag{7}$$

where $\hat{x}$ and $\hat{y}$ are discrete symbols obtained by organising the signals $x(t)$ and $y(t)$ according to trends in amplitudes of k time samples separated by a temporal separation of elements τ.

2.3 Clustering analysis

The features were computed for all channels for the spectral and complexity measures, for all pairs of channels for the connectivity measures, for each 30-sec segment, and subsequently normalised. This generates a feature matrix of size 1487×7 used as input to two clustering analysis methods. Considering that the goal is to differentiate between NREM and REM sleep, the number of clusters N is set to 2. Soft-clustering approach was used so that each data point belongs to both clusters with different degrees of memberships, which sum is equal to 1. A value of 0 means that the data point is not representative of the cluster at all. In the context of this study, this would then mean that a value of 1 represent the REM sleep stage while all the values between 0 and 1 represent the deepness of sleep. The higher the values, the lightest the sleep. Two clustering analyses were used.

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On one hand, Fuzzy c-means (FCM) is similar to the K-means algorithm. Soft-clustering is obtained by introducing a fuzziness parameter $m = 2$ when computing the objective function J_m [19]. Likewise, the goal is to minimise J_m in Eq. 8

$$J_m = \sum_{i=1}^{D} \sum_{j=1}^{N} \mu_{ij}^m \|x_i - c_j\|^2, \tag{8}$$

in which, D: number of data points, N: number of clusters, μ_{ij}^m: degree of membership of x_i to j^{th} cluster, c_i: j^{th} cluster centre.

On the other hand, Gaussian mixture models (GMM) attempts to determine the statistical model of the data using a Gaussian mixture distribution [20]. The data is assumed to arise from a finite mixture of probability density functions:

$$f\left(\mathrm{x}_i, \Theta\right) = \sum_{g=1}^{K} \pi_g \Phi\left(\mathrm{x}_i / \mu_g, \Sigma_g\right) \tag{9}$$

where K: number of clusters, $\pi_g > 0, (g = 1, ..., K)$ and $\sum_{g=1}^{K} \pi_g = 1$: mixing proportions, $\Phi\left(\mathrm{x}_i / \mu_g, \Sigma_g\right)$ is the underlying component-specific density function with parameters $\mu_g, \sigma_g, g = 1, ..., K$. The parameters in Φ are estimated by the maximum likelihood optimisation, more precisely by using the iterative Expectation-Maximization (EM) algorithm [21]. The model in Eq. 9 generates ellipsoidal clusters centred at the mean vector μ_g, and σ_g controls the other geometrical properties of each cluster.

The results obtained from both clustering analyses are then averaged using Eq. 10 to obtain a final unique value [22] that will determine the sleep stage of the patient.

$$P_{avg}(c, m_1 m_2) = avg(P(c, m_1), P(c, m_2)) \tag{10}$$

in which $P(c, m_1)$ (resp. $P(c, m_2)$) is the probability that the observation i is a member of cluster c in partition m_1 (resp. m_2).

3 Results

In this paper, an approach initially meant to assess consciousness levels in DoC and CLIS patients was slightly modified to determine sleep stages (NREM vs REM) in one female CLIS patient. Different features were extracted from the EEG signals before analysing them using soft-clustering approaches. Fig. 1 illustrates the obtained result. The general pattern of the plot resembles that of a healthy subject, with high predicted values before 00:00 (median: 0.8895) and after 06:00 (median: 0.6877) suggesting wakefulness. Intermittent lower and higher values suggesting deep sleep (SWS) alternating with light sleep (wakefulness (REM)) were observed between 00:00 and 06:00 (min: 0.0088, median: 0.1263, max: 0.9843).

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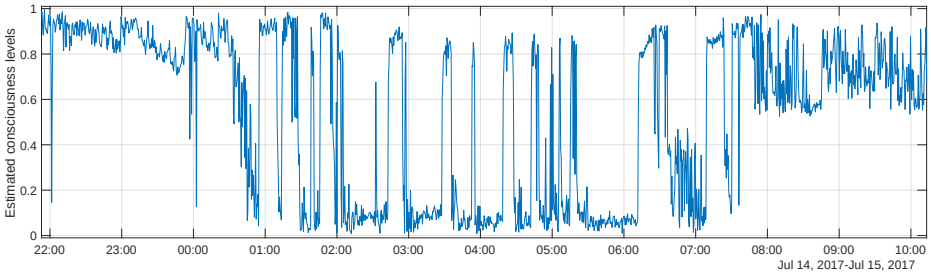

Fig. 1: Sleep stages of the CLIS patient. 0: deep sleep, 1: wakefulness.

4 Discussion and Conclusion

In healthy subjects, Slow-Wave Sleep (SWS) occurs during the deepest sleep stage (NREM) [2]. What was observed between 00:00 and 06:00 in Fig. 1 could consequently be interpreted as REM sleep alternating with SWS. This is confirmed by the analysis performed on the same patient in [3], which indicated that slow waves appeared from 02:00 and were followed by periods during which inactive wakefulness (REM) were observed. These observations imply a seemingly functional circadian system. When impaired, the latter could limit the patients' capabilities to communicate [1]. This patient was able to successfully use a functional Near-Infrared Spectroscopy (fNIRS)-based brain-computer interface (BCI) to communicate between 2014 and 2015. Moreover, when estimating her consciousness levels during some experiments using her EEG recordings, it was determined that the values were sufficient to initiate communication [7].

The results obtained using an adapted version of the approach to detect consciousness in patients with DoC and CLIS suggest its usability to also evaluate sleep stages in CLIS patients. This patient displayed a relatively normal sleep-wake cycle, which in turn indicates increased communication capabilities. Being able to communicate have been shown to increase CLIS patients' quality of life, thus contributing positively to the patient's mental well-being. One crucial shortcoming is however the lack of more data to validate these results.

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