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# Classifying subclinical depression using EEG spectral and connectivity measures

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*Abstract*— **Detecting depression on its early stages helps preventing the onset of severe depressive episodes. In this study, we propose an automatic classification pipeline to detect subclinical depression (i.e., dysphoria) through the electroencephalography (EEG) signal. To this aim, we recorded the EEG signals in resting condition from 26 female participants with dysphoria and 38 female controls. The EEG signals were processed to extract several spectral and functional connectivity features to feed a nonlinear Support Vector Machine (SVM) classifier embedded with a Recursive Feature Elimination (RFE) algorithm. Our recognition pipeline obtained a maximum classification accuracy of 83.91% in recognizing dysphoria patients with a combination of connectivity and spectral measures. Moreover, an accuracy of 76.11% was achieved with only the 4 most informative functional connections, suggesting a central role of cortical connectivity in the theta band for early depression recognition. The present study can facilitate the diagnosis of subclinical conditions of depression and may provide reliable indicators of depression for the clinical community.**

## I. Introduction

Depression severely affects both psychological and physiological functioning and has been defined as a leading cause of disease burden worldwide [1]. Accordingly, an accurate and early identification would be crucial to avoid treatment failure and symptoms exacerbation.

To date, in the clinical practice, a formal diagnosis of a mental health condition, such as depression, is usually supported by the use of semi-structured diagnostic interviews and validated questionnaires. However, these methods suffer from subjectivity biases that may result in a substantial reduction of diagnostic accuracy [2]. Given these premises, integrating neurophysiological measures within the standardized diagnostic screening procedure could have a significant impact on its early and objective detection and treatment.

In recent years, electroencephalogram (EEG) has been used as a noninvasive and inexpensive method to study depression-related neurophysiological changes. Depression has been linked to distinct resting-state power spectrum and functional connectivity dynamics, as compared to healthy individuals [3], [4]. Numerous studies have linked depression to higher resting-state alpha and theta frequency power in posterior sites as compared to controls [5], [6]. Moreover, recent evidence suggests that depression-related pathophysiological changes occur across networks of brain regions rather than within single clusters [7]. Particularly, increased functional connectivity within the theta and alpha frequency bands in a distributed network of anterior and poster brain regions has been reported in individuals with depression as compared to controls [3], [8].

Aiming for objective depression identification, machine learning models, e.g., back propagation neural network [9] and random forest classifier [10], have been applied to features extracted from the EEG data [11], [12]. A combination of spectral and nonlinear features has shown 87% of accuracy in discriminating 86 patients with depression from 92 healthy matched controls with k-nearest neighbor classifier [13]. Furthermore, functional connectivity measures estimated from different algorithms (e.g., synchronization likelihood [14], coherence measure [15] and phase lagging index [16]) were also able to classify individuals with depression from healthy controls with good performance.

Although, the aforementioned studies achieved promising results in automatically recognizing individuals already suffering from major depressive symptoms, more attention should be focused on advancing research for the early recognition and prevention of depression. A promising approach to identify individuals at risk of developing major depression is studying the subclinical depressive symptoms. Particularly, dysphoria, or subclinical depression, refers to a condition characterized by elevated depressive symptoms without meeting the criteria for a formal diagnosis of major depression according to the number, duration and impact on the functioning of symptoms [17].

In our earlier study [8], we have found higher functional connectivity within alpha and theta bands in individuals with dysphoria compared to healthy controls. Yet, to date, attempts for designing an automated method to classify the EEG dynamics of dysphoria population from healthy control group are lacking in the literature.

In this study, we propose an automatic approach to distinguish subclinical depression from healthy controls using EEG signals from 26 subjects with dysphoria and 38 healthy control group. As an extension to our previous work [8], we investigated features from spectral domain and brain connectivity from seven selected clusters of brain regions within the alpha and theta bands. We applied the support vector machine (SVM) classifier embedded with Recursive Feature Elimination (RFE) for the classification of the two groups [18]. We provide classification results in terms of sensitivity, specificity and accuracy of the recognition conducted with the inclusion of various feature sets to highlight the specific features leading to the highest recognition result.

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## II. Materials and Methods

### A. Subjects Recruitment, Experimental protocol and Acquisition set-up

A total of 64 female undergraduate students (average age of 22) completed a paper-and-pencil version of the Beck Depression Inventory-II [19]. Given the high female preponderance in dysphoria patients [20] and the stronger association of spectral changes and depression in women [21], only female participants were recruited.

Subjects with dysphoria were identified as those who scored at least 12 on the BDI-II test and had at least two current depressive symptoms for at least two weeks without meeting the diagnostic criteria for major depression, dysthymia or bipolar disorder as assessed by the mood episode module (module A) of the SCID-I [22]. Participants scoring equal to or less than 9 on the BDI-II, without current depressive symptoms as assessed by the SCID-I, were included in the healthy control group. As a result, the final dataset included 38 healthy control participants and 26 participants with dysphoria.

Participants were asked not to drink alcohol the day before the session and to avoid coffee and nicotine on the day of the experiment. None of the participants took antidepressants. Upon arrival at the laboratory, participants were seated in a quiet, dimly lit room and their EEG activity was acquired under eyes-open resting condition over a 4-minute period of each participant. They were asked to gaze at a fixation cross to minimize the eye movements and ocular artifacts. The EEG electrodes were placed on the scalp at standard position from 32 scalp positions using an Electro-Cap (Electrocap, Inc.) with tin electrodes. The signals were acquired with the sampling frequency of 500 Hz.

All participants gave their informed consent before being enrolled in the study. The study was approved by the local Ethics Committee, University of Padua (prot. No. 1407). The present study was conducted within an extensive research project, and most of the participants' data have also been described in previous publications [8], [23]–[26].

### B. Pattern recognition: Signal Processing, Feature extraction, and Classification

**Signal processing**: The data was filtered using a band-pass Butterworth filter between 0.5 Hz and 45 Hz. Then, principal component analysis was applied to identify the bad channels. The components associated with eye-blinks were identified by visual inspection and removed after applying the independent component analysis [27]. At the end, the signals were visually inspected to remove all the remaining artifacts related to movement or other noise sources [27].

To reduce the data dimensionality and mitigate the risk of over-fitting in further analysis, we grouped the 30 EEG channels (the two mastoids were excluded from the analysis) into seven clusters which were our regions of interest as following: *Cluster 1*: [F7, FP1, F3, FT7, FC3]; *Cluster 2*: [F8, FP2, F4, FT8, FC4]; *Cluster 3* : [T3, C3]; *Cluster 4*: [T4, C4]; *Cluster 5*: [P7, P3, O1, CP3, TP7]; *Cluster 6*: [P8, P4, O2, TP8, CP4]; *Cluster 7*: [FZ, CZ, PZ, FCZ, CPZ, OZ].

We averaged among the EEG channels in each cluster to obtain a new time series that represents the EEG information of that particular cluster related to our regions of interest.

**Feature extraction**: EEG features were extracted by means of spectral analysis, to quantify the brain activity, and functional connectivity analysis. The EEG power spectral density was derived by computing the Welch periodogram for each cluster time series on window segments of 4 seconds with 75% of overlap [28]. The resulting time-frequency spectral representation of the time series in each of the 7 regions for each subject was integrated within the theta (4-7 Hz) and the alpha (8-12 Hz) bands [29].

We applied a functional connectivity analysis to estimate the brain connectivity by calculating the neural synchrony between each pair of channels among the 7 selected regions for each subject. Particularly, we applied the mean phase coherence (MPC) index to quantify the phase synchronization between two time series [30]. The MPC index between two time series ($x(t)$,$y(t)$) is defined as follows:

$$MPC^2 = E[cos(\Delta(\phi))]^2 + E[sin(\Delta(\phi))]^2 \qquad (1)$$

where $E$ is the expectation operator and ($\Delta(\phi)$) is the relative phase difference obtained by subtracting the instantaneous phases of the two time series which are calculated from the analytical signal using the Hilbert transform [31]. In case of high phase synchronization between the EEG clusters, the MPC value is close to 1 while it is close to zero in case of weak synchronization [15].

We group the features obtained from the spectral and connectivity quantification of EEG channels into three feature sets.

- *Feature Set 1* = $\text{EEG}_{spectral}$ = $[\theta_{C_i}, \alpha_{C_i}]$
- *Feature Set 2* = $\text{EEG}_{mpc}$ = $[\theta_{C_i,C_j}, \alpha_{C_i,C_j}]$
- *Feature Set 3* = [$\text{EEG}_{spectral}$, $\text{EEG}_{mpc}$].

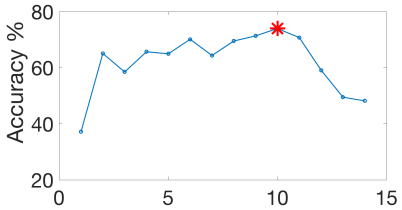
where $i, j = 1, \ldots, N$ and $N$ represents the number of clusters.

**Classification**: The classification aimed at discriminating between the individuals with dysphoria and the healthy control participants. Since the dataset contained a large number of features compared to the number of observations, it is important to reduce the dimensionality of the dataset by applying a feature selection algorithm. Accordingly, we applied a nonlinear SVM model with radial basis kernel along with an embedded feature reduction strategy (i.e., RFE algorithm). The SVM-RFE ranks the features by removing iteratively the feature that has the least impact on the SVM weight-vector norm. The result is the identification and selection of a subset of features that optimizes the performance of the SVM classifier [15]. The RFE is considered an embedded feature selection method, because the search of the optimal subset is built into the classifier construction and, therefore, is part of the learning process of the classifier. We specifically chose an embedded feature selection method because they have been proven to provide the best performance compared to other strategies due to their reduced computational cost and reduced over-fitting risk [32].

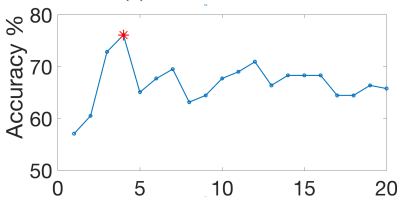
In addition, to perform an unbiased performance evaluation, we applied the Leave-One-Subject-Out (LOSO) validation scheme as a cross validation technique. Through this technique, having $N$ number of subjects, at each iteration the model is trained on feature set from $N-1$ subjects and tested on the feature sets from the left-out subject.

TABLE I: Ranked feature list using each feature set for recognition of dysphoria group from healthy control.

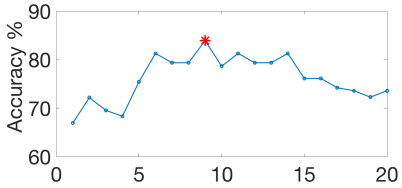
| Rank | Feature in *Feature set 1* | Feature in *Feature set 2* | Feature in *Feature set 3* |
|---|---|---|---|
| 1 | $\theta_{C1}$ | $\theta_{C1,C4}$ | $\theta_{C3,C2}$ |
| 2 | $\theta_{C6}$ | $\alpha_{C4,C2}$ | $\alpha_{C4,C2}$ |
| 3 | $\alpha_{C6}$ | $\theta_{C3,C2}$ | $\theta_{C5,C4}$ |
| 4 | $\theta_{C7}$ | $\theta_{C7,C4}$ | $\theta_{C4,C1}$ |
| 5 | $\alpha_{C4}$ | | $\theta_{C4}$ |
| 6 | $\theta_{C5}$ | | $\theta_{C1}$ |
| 7 | $\alpha_{C1}$ | | $\alpha_{C5,C4}$ |
| 8 | $\alpha_{C2}$ | | $\theta_{C3}$ |
| 9 | $\theta_{C2}$ | | $\alpha_{C4,C1}$ |
| 10 | $\alpha_{C5}$ | | |




(a) *Feature set 1*




(b) *Feature set 2*




(c) *Feature set 3*

Fig. 1: Classification results in terms of accuracy (%) on validation set as function of feature ranking selection implemented through the SVM-RFE-LOSO classifier using a) *Feature set 1* b) *Feature set 2* and c) *Feature set 3*. The x axis represents the number of features in each feature set.

TABLE II: Confusion matrix of dysphoria versus control classification using spectral features.

| Feature set 1 (spectral) | Healthy group | Dysphoria group |
|---|---|---|
| Healthy group | 76.92 % | 28.95 % |
| Dysphoria group | 23.08 % | 71.05 % |

Recognition accuracy: 73.99 %

TABLE III: Confusion matrix of dysphoria versus control classification using connectivity features.

| Feature set 2 (connectivity) | Healthy group | Dysphoria group |
|---|---|---|
| Healthy group | 65.38 % | 13.16 % |
| Dysphoria group | 34.62 % | 86.84 % |

Recognition accuracy: 76.11 %

TABLE IV: Confusion matrix of dysphoria versus control classification using spectral and connectivity features.

| Feature set 3 (all) | Healthy group | Dysphoria group |
|---|---|---|
| Healthy group | 73.08 % | 5.26 % |
| Dysphoria group | 26.92 % | 94.74 % |

Recognition accuracy: 83.91 %

## III. Results

In this section classification results for discriminating individuals with dysphoria from healthy controls are reported. The classification procedure is performed on the three feature sets defined in Section II-B. The recognition accuracy as a function of number of features from *Feature set 1*, *Feature set 2* and *Feature set 3* are depicted in Figures 1a, 1b and 1c, respectively. Table I shows the ranking of the selected feature subset that led to the maximum performance considering each feature set. Moreover, the confusion matrices associated with the best recognition accuracy from each feature set are shown in Tables II, III and IV, respectively. The diagonal values of this matrix corresponds to the sensitivity and specificity of the classification.

The results show that recognition accuracy of 73.99 % (sensitivity=76.92% and specificity=71.05%) and 76.11 % (sensitivity=65.38% and specificity=86.84%) is achieved using only features from spectral and connectivity analysis, respectively.

However, the highest accuracy (83.91% (sensitivity=73.08% and specificity=94.74%) is obtained while considering all the features present in *Feature set 3*. This accuracy is obtained through 9 features comprising of MPC indices in theta band between C3-C2;C5-C4;C4-C1 and in alpha band between C4-C2;C5-C4;C4-C1 as well as power spectrum estimates of C1,C3,C4 regions within theta band. The best recognition result using *Feature set 1* is obtained through 10 out of 14 features while only 4 features in *Feature set 2* contributed to the best recognition.

## IV. Discussions and Conclusions

In the present study, we proposed a pattern recognition pipeline for recognizing the neurophysiological patterns of dysphoria from the resting state EEG activity. Spectral and functional connectivity estimates were evaluated both separately and in a combined feature sets for both theta and alpha frequency bands.

The choice of the SVM classifier embedded with RFE feature reduction is, firstly, to reduce the data structure complexity to avoid the risk of over-fitting that rises while training the classifier with a relatively large feature set and, secondly, to identify the most influential feature subset that achieves the maximum classification performance. Moreover, the LOSO validation scheme allows building an unbiased subject-independent classification.

The results show that the best classification performance (83.91% of accuracy) is obtained while combining the spectral and functional connectivity measures (*Feature Set 3*). This confirms the importance of different sources of information (spectral and connectivity analyses) for quantifying the neural dynamics. On the other hand, it is important to consider not only the estimated accuracy but also the generalization performance. This refers to the performance on out-of-sample data of the models learned by the learning algorithm. In this regard, the model with the best trade-off between accuracy and robustness is probably obtained considering only the functional connectivity features. Indeed, in *Feature Set 2*, only 4 features contributed to the highest classification performance achieving 76% of accuracy. Instead, the spectral feature set (*Feature Set 1*) does not offer a great performance (73.99% of accuracy) considering the

number of selected features (9 out of 14). Of note, both *Feature Set 2* and *Feature Set 3* encompassed functional connectivity within theta frequency band in a fronto-centro parietal network as a major contributor to the robustness of the model. This is in line with previous studies showing selective changes within the theta frequency band in individuals with depressive symptoms [3], [5], [8], and possibly indicate functional impairment in the limbic system of individuals with dysphoria, which has been shown to be related mostly to theta frequency band in the human cortex [33]. Hence, the present results might indicate that functional connectivity within theta frequency band is an independent and robust indicator of dysphoria, as also supported by our previous work [8].

In conclusion, this study tackles the challenge of early identification of depression by suggesting an automatic way to effectively identify dysphoria through neurophysiological measures. Our results suggests that a combination of both EEG spectral and, mainly, connectivity measures within the theta frequency band may provide important information for early identification of depression. In future studies, we aim to increase the number of subjects and explore other connectivity metrics for quantifying causal interactions and cortical sources associated with dysphoria, expanding the research also towards emotional tasks.

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