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On the Deconvolution Analysis of Electrodermal Activity in Bipolar Patients

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***Abstract*—People affected by bipolar disorders experience alternating states of depression with episodes of mania or hypomania. This mental can lead to a poor handling of daily routines, can worsen personal relationships, and often can be life-threatening. This preliminary study aims at investigating how the autonomic nervous system, in terms of electrodermal activity, responds to specific controlled emotional stimuli in bipolar patients. More specifically, we present here a method to deploy the analysis of ElectroDermal Activity (EDA) to discriminate clinical mood states. EDA was analyzed by using a deconvolution method to separate tonic from phasic components. The three subjects recruited and the experimental protocol used here is part of the European project PSYCHE. Preliminary results show that the bipolar mood states can be related to electrodermal tonic activity.**

I. Introduction

Millions of people in Europe and in the United States (see the epidemiological study in [1]) are affected by the bipolar disorder. The bipolar disorder is characterized by a mood fluctuation ranging from depression to mania, and it is generally accompanied by anxiety. Sometimes, patients also experience both symptoms of depressive and maniac states repetitively in a very short time, and this is defined as "mixed-state". Normal mood is referred to as "euthymic" state. Referring to anxiety, it can be associated with bipolar disorder in two modalities either as a symptom of the bipolar disorder itself or as a separate anxiety condition in addition to the bipolar disorder [2]. In current clinical practice settings patients' mood is assessed through clinician-administered rating scales and questionnaires, such as the Bauer Internal Mood Scale, the Hamilton Scale for Depression and the Young Mania scale. Physiological parameters are not used for this purpose. Previous research has shown a relation between Autonomic Nervous System (ANS) dysfunctions and the bipolar disorder. Specifically, studies on sleep [3],and circadian heart rate rhythms [4] showed to be sensitive to clinical states in such a way that these parameters may be considered predictors of clinical changes. Moreover in the literature, it is known that an electrodermal hypoactivity is present during depression in both unipolar and bipolar patients. This condition is stable over time, and does not appear to depend on experimental conditions or stimulus characteristics [5]. In this work, three patients were recruited for the study, which is part of the European project PSYCHE (Personalised monitoring SYstems for Care in mental HEalth), which is funded in the Seventh Framework Programme. In the PSYCHE project, patients wear a sensorized T-shirt based on textile electrodes during normal daily activities. The sensorized shirt allows the acquisition of the ElectroCardioGram (ECG) and ReSPiration (RSP) signals. In addition to daily activity monitoring, a specific protocol for the evaluation of emotional responses is administered, in which ECG, RSP and EDA are acquired. This work aims at exploiting EDA changes for assessing the patient's mood state during the emotional stimulation, and for investigating mood fluctuations over a period of 75 days. The rationale behind this work is that, as EDA is directly related to the Sympathetic Nervous System (SNS) [6] and mood fluctuations affect the sympathetic activity, an EDA analysis can reveal change in the mood state. In order to evoke EDA we used pictures selected from the International Affective Picture System (IAPS) [7]) and tables belonging to the Thematic Apperception Test (TAT) [8]. The IAPS database is widely used for studies that assess emotional processing, and it comprised hundreds of pictures with associated a specific emotional rating in terms of arousal, valence, and dominance. Arousal refers to the emotional impact (positive or negative) of the image, valence refers to pleasant or unpleasant feelings induced by the the image, while dominance indicates if the subject feel emotionally dominant or dominated while looking at the image. The TAT is a projective psychological test. The TAT is supposed to reveal repressed aspects of personality. In this study the pictures were only used as a support for the production of free speech by the patients. The IAPS pictures are expected to induce a changes in the SNS, and the TAT pictures are supposed to be emotion inducing stimuli.

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II. Materials and methods

Since EDA is related to changes in the skin conductivity, i.e. skin electrical properties, due to sweat glands activity, hereinafter, in this work we refers to EDA as Skin Conductance (SC). In this section, the experimental protocol and the deconvolution analysis for the SC will be reported.

A. Experimental protocol

Three patients were recruited for this preliminary study. None of them had suicidal tendencies, delusions or hallucinations. Patients were screened through a psychiatric interview and classified as "Euthymic", "Depressed" or "Mixed-state", to the state of the patients. In addition, a questionnaire was administered to the patients in order to evaluate their level

of anxiety. Two different levels of anxiety (i.e. low and high) were identified. The protocol was administered as following:

- 5 minutes of resting state with closed eyes;
- 5 minutes of resting state with open eyes;
- IAPS presentation: in which the subject looked at a sequence of images having different content of arousal and random valence (6 minutes);
- TAT presentation: in which the subject looked at and commented a sequence of images (about 4 minutes).

During the whole emotional elicitation protocol, the SC signal was acquired with the BIOPAC MP150 system. The protocol was administered during a 75 days-period. Each subject attended the same experiment when the mood state changed, based on a clinical evaluation. Subjects were identified with the abbreviations Pz01, Pz02 and Pz03. Pz01 and Pz03 performed the experiment two times, while the patient Pz02 performed the experiment five times. Hereinafter, each repetition of the protocol is called "Acquisition" (Acq.).

B. Deconvolution analysis

The SC signal is characterized by a slowly varying component called tonic component (i.e. Skin Conductance Level, SCL) and a superposed phasic component (Skin Conductance Response, SCR). SCR is strictly related to a given stimulus and is defined as the part of the signal which arises within a predefined response window ($1-5s$ after stimulus onset), satisfying a minimum amplitude criterion ($0.05\mu S$), [9], [10]. SCR is characterized by a short rise time followed by a slower recovery time. Generally, in the case of an inter-stimulus interval shorter than the SCR recovery time, an overlapping of consecutive SCRs is visible. It results in one of the main SC issue, since it does not allow a good estimation of responses as well as the signal division into its phasic and tonic components. In order to overcome the latter issue, we analyzed the SC by means of a modeling technique based on the deconvolution process, [11]. This method allows estimating the SudoMotor Nerve Activity (SMNA) which is a part of the SNS. More specifically, the SNS through the SMNA controls the eccrine sweat glands activity. The relation between SMNA and SCR is modeled by the following biexponential Impulse Response Function (IRF) also called Bateman function [12]:

$$IRF(t) = (e^{-\frac{t}{\tau_1}} - e^{-\frac{t}{\tau_2}}) \cdot u(t) \qquad (1)$$

where $u(t)$ is the stepwise function. The result of deconvolution between SC and IRF is defined as *driver function* which describes the SMNA behavior. The Bateman function is directly derived from bicompartment model of the diffusion process of the sweat through the sweat ducts (first compartment) and the stratum corneum (second compartment) [13]. The processing chain of SC data was constituted of five stages. Specifically, these stages are the preprocessing stage in which the signal was filtered to reduce the noise, the decomposition of the SC in its tonic and phasic component, the feature extraction, the statistical analysis to evaluate the statistical significance of the extracted feature associated to the mood, and finally the classification process for classifying the mood states of the patients. In the next paragraphs each stage is explained in detail.

1) Preprocessing: The preprocessing consists of two stages. The first stage is the detection and removal of the movement artifacts, it was carried out by manual cut off through a visual inspection. The second stage was a filtering with a low pass zero-phase forward and reverse digital filter [14], [15] with a cutoff frequency of 2 Hz, to limit the frequency bandwidth of electrodermal signal.

2) SC decomposition: The decomposition of the SC in its components was performed by means of Ledalab 3.2.2. software package for MATLAB [16]. In detail, SC data was described [11] as follows:

$$SC = (DRIVER_{tonic} + DRIVER_{phasic}) * IRF \qquad (2)$$

The sum of the two driver functions was achieved by a deconvolution between the skin conductance data and the impulse response function. According to the Eq. 2 the phasic driver was obatained subtracting the tonic from the deconvoluted signal. The hypothesis underling SC component behaviors is that tonic activity is observable in the absence of any phasic activity [6]. Therefore, the tonic component was obtained by the application of a smoothing Gauss window of $200ms$ and a peak detection algorithm in order to find the peaks over a threshold of $0.2\mu S$ (e.i. all the peaks over the threshold were identified as a part of the phasic response), and the points under the threshold were considered as part of the tonic driver. In order to estimate the continuous tonic driver signal the points detected were used to build a 10-s spacing grid and then the grid points were interpolated with a cubic spline fitting method. As mentioned above, the phasic driver is the result of the subtraction between the continuos tonic and the deconvoluted signal. As shown in fig. 1 the original SC signal and the two deconvoluted tonic and phasic driver signals, during resting and elicitation states, are reported).

3) Feature extraction: Features were extracted from both tonic and phasic driver signals. The extracted features were the mean value, maximum value and Area Under the Curve (AUC) of the driver signals within a window response of $5s$. In particular AUC is conceived as an optimum indicator of sympathetic activity [11].

4) Statistical analysis: An intra-subject statistical inference analysis was performed by means of non parametric tests due to the non-gaussianity of the sample sets. Concerning subjects Pz01 and Pz03, the features of each pair of acquisition were compared by a Rank-Sum test to show whether the data belonged to the same population or not. The Subject Pz02 had more than two available acquisitions. Therefore a multiple comparison analysis applying the Mann-Whitney U-test with a Bonferroni adjustment for every pair of Pz02's acquisitions was carried out. The procedure was repeated for both the tonic and phasic driver features.

5) Classification: The classification process was used to perform a recognition of the clinical mood states (i.e. depression state, mixed-state and euthymic state). In order to

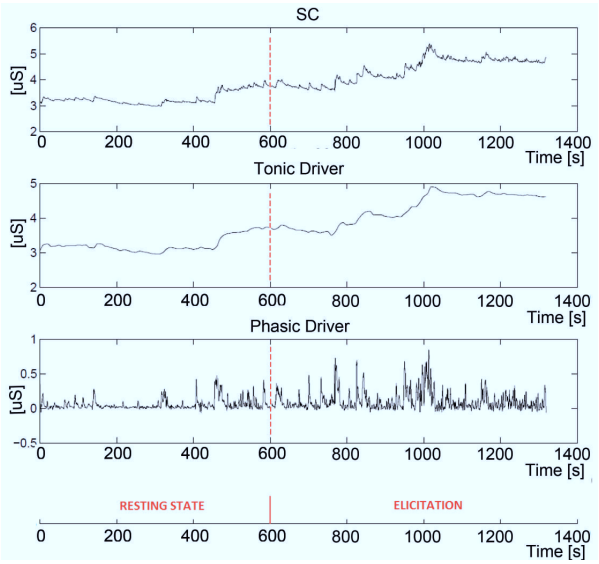

Fig. 1. Example of decomposition analysis. In the upper figure the SC signal before the deconvolution analysis is reported. The lower figures report the deconvoluted tonic and phasic driver signals during resting and elicitation phase.

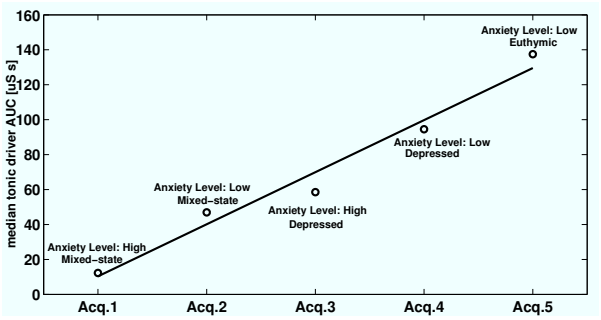

Fig. 2. Linear regression of tonic-driver-AUCs of Pz02

TABLE II
CONFUSION MATRIX OF DEPRESSION STATE VS EUTHYMIC STATE

	Euthymic	Depressed
Euthymic	90.50 ± 1.89	11.69 ± 1.54
Depressed	9.50 ± 1.89	88.31 ± 1.54

TABLE III
CONFUSION MATRIX OF K-NN CLASSIFIER FOR MIXED-STATE VS EUTHYMIC STATE

	Euthymic	Mixed-state
Euthymic	76.22 ± 3.11	18.73 ± 3.24
Mixed-state	23.78 ± 3.11	81.27 ± 3.24

TABLE IV
CONFUSION MATRIX OF K-NN CLASSIFIER FOR MIXED-STATE VS DEPRESSED STATE

	Depressed	Mixed-state
Depressed	82.08 ± 2.82	16.91 ± 2.37
Mixed-state	17.92 ± 2.82	83.09 ± 2.37

perform the classification we used a K-Nearest Neighbor (K-NN) classifier. It predicts the class finding the k closest training points, and the new example is assigned to the class most common amongst its k nearest neighbors. After the training process, the performance of the classification task is commonly evaluated using the confusion matrix. A more diagonal confusion matrix corresponds to a higher degree of classification. The training phase is carried out on 80% of the feature dataset while the testing phase to the remaining 20%. We performed 40-fold cross-validation steps in order to obtain unbiased classification results, i.e. it allowed us to consider as gaussian the distribution of classification results, which can be therefore described as mean and standard deviation among the 40 obtained confusion matrices.

III. RESULTS

The clinical evaluations of the patients under examination are shown in table I. The Mann-Whitney test was performed on the features extracted from the phasic driver signal, in order to compare the two acquisitions of both patients Pz01 and Pz03. A p-value less than 10^{-6} showing a strong statistical difference was obtained. A Kruskal-Wallis test was performed on the acquisitions of subject Pz02 showing that the null hypothesis of equal medians among the acquisitions can be rejected with a p value less than 10^{-6}. A post-hoc test using Bonferroni adjustment was carried out to investigate on all pairwise comparisons. All the pairs resulted statistically different with a p-value less 10^{-6}. Similar results were achieved analyzing the features extracted from the tonic driver signal of patients Pz01, Pz03. It was obtained, indeed, a strong statistical difference with a p-value less than 10^{-6}. Kruskal-Wallis test on the acquisitions of subject Pz02 showed that at least one acquisition was statistically different from the others, while the post-hoc test with Bonferroni adjustment showed that there were statistically significant differences among all pairs of acquisitions (with a p value less than 10^{-6}) except for the pair Acq.4 vs. Acq.5 ($p = 0.108$). Moreover, among the features, AUC of the tonic driver (tonic-driver-AUC) showed an interesting behavior across the different acquisitions on Pz02. Fig. 2 reports the median tonic-driver-AUC versus the different acquisitions. Already at a glance it is worthwhile noting a linear monotonic trend, which is confirmed by a linear regression analysis which provided a correlation coefficient of 0.9886 and a p-value of 0.0015. An inter-subject analysis was performed grouping those acquisitions with the same clinical label. The features corresponding to the three groups, i.e. *Depressed*, *Mixed-state* and *Euthymic*, were used as dataset for a pattern recognition by means of the K-NN classifier. More in detail, K-NN classifier was used as supervised machine learning to solve the two class problem for the recognition of Euthymic vs Depressed (see Table II), Euthymic vs Mixed-state (see Table III) as well as Depressed vs Mixed-state (see Table IV), it is worthwhile noting that all classifications are greater than 76%.

TABLE I
CLINICAL EVALUATIONS OF THE PATIENTS

	Acq.1		Acq.2		Acq.3		Acq.4		Acq.5	
	Mood state	Anxiety	Mood state	Anxiety	Mood state	Anxiety	Mood state	Anxiety	Mood state	Anxiety
Pz01	Depressed	High	Euthymic	Low	x	x	x	x	x	x
Pz02	Mixed-state	High	Mixed-state	Low	Depressed	High	Depressed	Low	Euthymic	Low
Pz03	Mixed-state	High	Depressed	Low	x	x	x	x	x	x

IV. CONCLUSION AND DISCUSSION

In this preliminary study we analyzed electrodermal activity (i.e. SC) over a 75 days-period in three bipolar patients recruited in the frame of the European project PSYCHE. For each patient, mood state fluctuated at least once along with a change in the anxiety level. Two patients were monitored with two acquisitions and one subject with five acquisitions. A deconvolution analysis was applied to the SC signal. Several features were extracted in order to quantify the phasic and tonic electrodermal activity. The preliminary results showed a statistically significant difference for all the acquisitions from the same subject, which is consistent with the corresponding clinical diagnosis. More specifically, for the subjects Pz01 and Pz03 that had only two acquisitions, in two different mood states, statistical test showed that both mood states were effectively recognized as statistically different. Instead referring to the subject PZ02, who underwent five acquisitions, each state was recognized as statistically different according to the different mood states and anxiety levels. Only between Acq.4 and Acq.5 of subject Pz02 the Mann-Whitney test showed a p-value greater than 0.05 for the features extracted from the tonic driver component. Acq.4 and Acq.5 had two different clinical labels but the same level of anxiety, but they resulted to be equivalent from a statistical point of view. This may result from the very short time-window occurring between the two acquisitions (six days only) or by the same anxiety level. Much work has to be done in order to gain a closer understanding on this aspect. Moreover, subject Pz02 showed a monotonic trend of tonic-driver-AUC which is the component that is not related to the stimulus. In particular, the transition from the mixed-state with a high level of anxiety (2) to the euthymic state with a low level of anxiety (1) showed a linear trend modeled through a linear regression with a high correlation coefficient. Even in this case, this behavior, although very interesting, deserves to be investigated more in depth. Nevertheless, in the other subjects (who had only two acquisitions available, i.e. a number insufficient for a linear regression model) tonic electrodermal activity showed an increase in the presence of a mood change from a depressed state to an euthymic state and from a mixed-state to a depressed state, combined with a lower level of anxiety. An inter-subject analysis was performed attempting to classify the acquisitions accompanied by the label *euthymic*, *depressed* and *mixed-state* by means of a pairwise comparison between the three class. All the three possible comparisons showed a high discrimination percentage ($> 76\%$). The preliminary results support the hypothesis of a relationship between mood state, anxiety level and electrodermal activity. Although preliminary these results are very satisfactory and encouraging. Future work will include a wider patients' sample and a higher number of acquisitions in order to improve the statistical significance of results.

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