Electrodermal activity in bipolar patients during affective elicitation

Electrodermal Activity in Bipolar Patients during Affective Elicitation

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***Abstract*—Bipolar patients are characterized by a pathological unpredictable behavior, resulting in fluctuations between states of depression and episodes of mania or hypomania. In the current clinical practice, the psychiatric diagnosis is made through clinician-administered rating scales and questionnaires, disregarding the potential contribution provided by physiological signs. The aim of this paper is to investigate how changes in the autonomic nervous system activity can be correlated with clinical mood swings. More specifically, a group of ten bipolar patients underwent an emotional elicitation protocol to investigate the autonomic nervous system dynamics, through the electrodermal activity (EDA), among different mood states. In addition, a control group of ten healthy subjects were recruited and underwent the same protocol. Physiological signals were analyzed by applying the deconvolutive method to reconstruct EDA tonic and phasic components, from which several significant features were extracted to quantify the sympathetic activation. Experimental results performed on both the healthy subjects and the bipolar patients supported the hypothesis of a relationship between autonomic dysfunctions and pathological mood states.**

***Index Terms*—Bipolar disorder, deconvolutive analysis, electrodermal activity (EDA), mood recognition.**

I. Introduction

BIPOLAR disorder is a chronic illness involving millions of people in Europe and in the United States (see the epidemiological study in [1]). Patients experience mood swings whose symptoms can be associated to one of the following psychophysiological states: depressive, maniac, mixed, and euthymic. During depressive episodes, patients feel sad and, sometimes, desperate. Other neurovegetative symptoms including loss of appetite and sleep are also present. Depressed patients might also experience thoughts of ruin, guilt, or death including suicidal thoughts that might lead to suicide attempts. During manic episodes, patients are hyperactive, and often experience a reduction of the need to sleep. Mixed states are characterized by both depressive and hyperactivity symptoms. In the intervals between these episodes, patients typically experience periods of relatively good emotional balance (labeled as euthymia). Moreover, mood swings are also usually accompanied by anxiety, which is associated with bipolar disorder either as a symptom of the bipolar disorder itself or as a separate pathological condition [2].

In spite of the great impact on the population and healthcare costs, current clinical practice still relies only on the physician expertise, rating scales and questionnaires, such as the Bauer Internal Mood Scale, the Hamilton Scale for Depression, and the Young Mania scale [3]. Physiological parameters (e.g., biological markers, physiological signals, etc.) are not taken into account for diagnosis or follow-up purposes [4]–[6]. As a matter of fact, there is the need of more objective parameters for the diagnosis of mental disorders. Mental disorders are long-term illnesses and may remain undetected for years before they are properly diagnosed and put under treatment. Moreover, patients are extremely heterogeneous with respect to the phenomenology and severity of symptoms, number, and duration of episodes, as well as the time interval between them. Finally, other disorders may also be present (i.e., comorbidity).

Previous research has shown a link between the autonomic nervous system (ANS) dysfunctions and bipolar disorder [7]–[12]. Specifically, studies on sleep [13], voice analysis [14], and circadian heart rate rhythms [15], [16] showed to be sensitive to changes in the clinical state, suggesting that these parameters may be considered as markers of clinical change. Moreover, it is known that electrodermal hypoactivity is present during depression in both unipolar and bipolar patients [17], [18]. This condition is stable over time, and does not appear to depend on experimental conditions or stimulus characteristics [19]. In a recent study, we demonstrated that a single variable approach is not a reliable method for characterizing mood swings in bipolar patients while using heart rate variability and respiration activity series [10], [12]. Nevertheless, a complete and comprehensive ANS characterization should also rely on other physiological signals that are strictly related to the sympathetic nerve activity such as the electrodermal activity (EDA). In the present study, we investigated EDA dynamics in bipolar patients during an emotional stimulation paradigm. Since the changes on EDA are directly related to the sympathetic activity [20], EDA analysis could serve as an effective ANS marker for characterizing different mood states.

The stimulation protocol proposed in this paper is based on displaying pictures selected from the international affective

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picture system (IAPS) [21]) and pictures from the thematic apperception test (TAT) [22]. They were presented to the patients in order to elicit emotional reactions. The IAPS database is widely used for studies that assess emotional processing (e.g., see previous studies in [23]–[27]), and it is comprised of hundreds of pictures which associated a specific emotional rating in terms of arousal and valence. Arousal refers to the physiological activation that is elicited by an emotionally salient image resulting in a subjective state of calmness or excitement. Valence refers to the experience of pleasantness or unpleasantness induced by viewing the image. The TAT is a projective psychological test that is supposed to reveal repressed aspects of personality. Such an experimental protocol was administered to ten bipolar patients as well as ten healthy subjects. Concerning the methodology of signal processing, we used a deconvolutive approach [28] in order to retain consecutive sympathetic responses which can be overlapped whenever the interstimulus interval is shorter than the previous one.

Similarly to our previous investigation [10], [12], the present study was carried out in the frame of the European project PSYCHE, which stands for personalized monitoring systems for care in mental health. Within this project, a personalized, pervasive, cost-effective, and multiparametric monitoring system based on textile platforms and portable sensing devices was devised for the long-term and short-term analysis of mood disorders [10], [12], [14], [29].

II. Materials and Methods

A. Patient Recruitment and Experimental Protocol

Ten patients affected by bipolar disorder I or II were selected for this study. None of them had suicidal tendencies, delusions, or hallucinations. Patients were admitted to the psychiatric unit of the hospital and periodically screened through a psychiatric interview. Before each acquisition, a mood label among "euthymic", "depressed", "maniac", and "mixed-state" was associated to each patient/acquisition. As a control group, a group of healthy subjects were enrolled and participate to the study. In particular, ten healthy subjects (five females, age ranged from 20 to 32), i.e., not suffering from both cardiovascular and evident mental pathologies, were asked to fill out the Patient Health Questionnaire^{TM}. All participants showed scores lower than 5. Such a cut-off value was chosen in order to avoid the presence of either middle or severe personality disorders [30].

An *ad hoc* affective elicitation experimental was administered to both the healthy and bipolar patients group. In particular, such an experimental protocol, graphically shown in Fig. 1, was structured as follows:

1) 5 min at rest with closed eyes;
2) 5 min at rest with open eyes;
3) 6-min slideshow of IAPS pictures with high arousal and negative valence;
4) up to 4 min of pictures gathered from TAT.

As described previously, the protocol is split into two sessions: rest and emotional elicitation. The latter session is divided, in turn, into two stages, both of which are intended to elicit a variation of the ANS response. Specifically, IAPS pictures lasted for 2 s presenting negative emotional contents (high arousal and negative valence). The same IAPS pictures were presented to all patients and healthy subjects and nobody was asked to score the elicited level of arousal and valence. The images were chosen according to the following characteristics: arousal score >6.7; valence <4.5. Afterwards, patients were invited to tell a story based on the input coming from the TAT pictures. However, in order to avoid biased results related to the IAPS and TAT sequential order, the IAPS–TAT and TAT–IAPS session orders were randomly interchanged. The hypothesis of this study is that the ANS differentially reacts to such emotional stimuli upon different pathological mood states. During the whole duration of the protocol, the EDA signal was acquired using the BIOPAC MP150 system with a sampling frequency of 1000 Hz. EDA sensors were placed on the distal phalanx of the second and third finger of the nondominant hand, imposing a dc voltage of 0.5 V. The protocol was run for a follow-up period of up to 75 days. Patients repeated the protocol at each mood change, whereas the healthy subjects repeated the experiment twice within two weeks in order to investigate possible differences in the EDA pattern between repeated acquisitions during no pathological mood states and swing. Of note, seven patients (i.e., Pz01, Pz02, Pz04, Pz07, Pz08, Pz09, and Pz10) were acquired twice, whereas Pz03, Pz05, and Pz06 carried out a single acquisition. Details are shown in Table I.

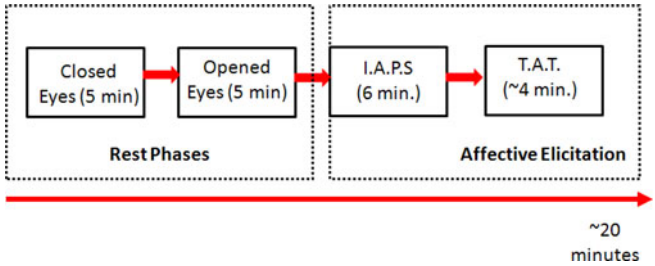

Fig. 1. Block scheme of the experimental protocol.

TABLE I
Clinical Evaluations of the Patients

	Acq.1	Acq.2
	Mood state	Mood state
Pz01	Depressed	Euthymic
Pz02	Depressed	Euthymic
Pz03	Mixed-state	N.P.
Pz04	Mixed-state	Euthymic
Pz05	Mixed-state	N.P.
Pz06	Depressed	N.P.
Pz07	Depressed	Euthymic
Pz08	Mixed-state	Euthymic
Pz09	Mixed-state	Euthymic
Pz10	Depressed	Euthymic

N.P. stands for Not Performed.

B. Methodology of Signal Processing

The EDA decomposition process consisted in three different steps: a preprocessing phase, in which the signal was filtered to reduce the noise, a deconvolution process in order to obtain the phasic and tonic driver, and an optimization stage to improve the estimation of the parameters of the impulse response function.

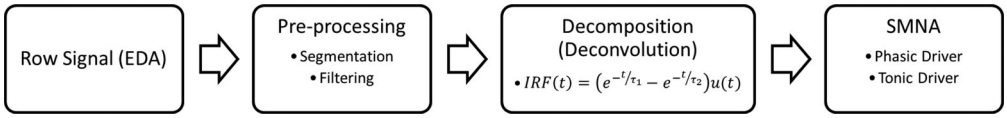

Fig. 2. Electrodermal acquisition and decomposition process. The EDA is filtered to reduce the noise and then decomposed in tonic and phasic components by means of a deconvolution with an IRF called the Bateman function.

The decomposition process was performed by means of Ledalab 3.2.2. software package for MATLAB [30].

1) Preprocessing: In the preprocessing stage, the detection of movement artifacts was carried out by visual inspection. Artifact-free signals exclusively were taken into account for further analysis. In order to limit the frequency bandwidth of the EDA signal, it was filtered with a low-pass zero-phase forward and reverse digital filter [31], [32] with a cutoff frequency of 2 Hz, having Buttworth approximation.

2) EDA Deconvolution Analysis: EDA is produced by changes in the skin conductivity as major effect of the sweat glands activity. Specifically, sweat is released to the sweat duct, passes to the stratum corneum, and finally is brought out of the skin. Accordingly, the dynamics of the variation of concentration of sweat in the stratum corneum can be represented by a two-compartment pharmacokinetic model in which the sweat concentration is assumed to change only by diffusion [33], [34]. The first compartment represents the sweat duct and the second compartment the stratum corneum. Due to the two compartments being different in dimension (i.e., the stratum corneum is much larger than the sweat duct), the diffusion can be considered as a one-way diffusion. Solving the two coupled first-order differential equations of each compartment, the solution is the impulse response function $\mathrm{IRF}(t)$ which is also known as the Bateman function [35]:

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

The Bateman function is characterized by a steep onset and a slow recovery. The steepness of onset and recovery is determined by the time constants τ_1 and τ_2.

EDA can be divided into tonic (SCL: Skin Conductance Level) and phasic components (SCR: Skin Conductance Response). The tonic electrodermal component represents the baseline level of the signal, whereas the phasic component indicates a direct response to a specific stimulus. However, there are often phasic parts of EDA which cannot be related to any specific stimulus, and hence, they are called spontaneous or nonspecific SCRs [20]. Sometimes, when the time interval between two consecutive stimuli is shorter than the recovery period of SCR, the stimuli responses in the SCR are overlapped. In this case, the typical shape of the SCR is lost and this could be one of the main issues for the extraction of the correct information from the electrodermal signal. In order to overcome this issue, the EDA signal process is modeled as a convolution process between the SudoMotor nerve activity (SMNA), as part of the sympathetic nervous system, and IRF [28] under the hypothesis that EDA is controlled by SMNA resulting in a sequence of distinct impulses which regulate the eccrine sweat glands dynamics (see Fig. 2).

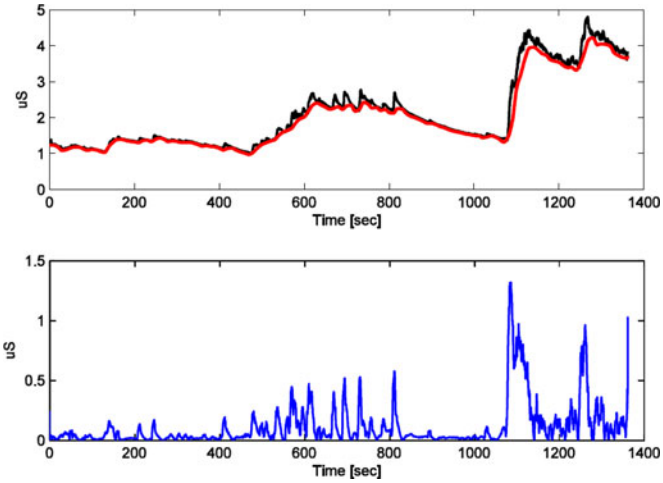

Fig. 3. Example of EDA signal and related components during euthymic state, extracted through deconvolutive method of analysis. On the top panel, the black signal representing the raw EDA signal along with the $\mathrm{DRIVER}_{\mathrm{tonic}}$ (red) are shown. On the lower panel, the $\mathrm{DRIVER}_{\mathrm{phasic}}$ is shown. Rest phases lasted for the first 600 s. Afterwards, IAPS and TAT emotional stimulation is performed.

Formally, it is possible to write:

$$\mathrm{EDA} = \mathrm{SMNA} \otimes \mathrm{IRF} \tag{2}$$

where $\mathrm{SMNA} = (\mathrm{DRIVER}_{\mathrm{tonic}} + \mathrm{DRIVER}_{\mathrm{phasic}})$. In (2), SMNA is unknown and it is evaluated by deconvolving the EDA signal with the IRF. In order to decompose the obtained SMNA signal into the $\mathrm{DRIVER}_{\mathrm{tonic}}$ and $\mathrm{DRIVER}_{\mathrm{phasic}}$ components, several algorithmic steps have been processed. A smoothing Gauss window of 200 ms is applied to SMNA, followed by a peak detection algorithm in order to find the peaks over a threshold of $0.2\,\mu$S. All the points below the threshold were interpolated with a cubic spline fitting method giving the $\mathrm{DRIVER}_{\mathrm{tonic}}$. More details can be found in [28]. Finally, the $\mathrm{DRIVER}_{\mathrm{phasic}}$ component, instead, is computed by subtracting the previously estimated $\mathrm{DRIVER}_{\mathrm{tonic}}$ from the SMNA (see Fig. 3), under the hypothesis that the tonic activity is observed in the absence of any phasic activity [20].

Of note, the $\mathrm{DRIVER}_{\mathrm{phasic}}$ signal should have a zero baseline intermitted by distinct peaks overcoming the issue of having overlapped SCRs.

3) Optimization: Starting from fixed values, the parameter set of the IRF (i.e., τ_1 and τ_2) was optimized according to criteria evaluating the quality of the model, through the minimization of a specific cost function given by the sum of the number of points of the $\mathrm{DRIVER}_{\mathrm{phasic}}$ component that have a negative value and the number of points above a predefined threshold (equal to 5% of the maximum of $\mathrm{DRIVER}_{\mathrm{phasic}}$). This procedure aims at

TABLE II
LIST OF THE FEATURES EXTRACTED FROM THE EDA PHASIC AND TONIC COMPONENTS

Feature	Description
MAX-Tonic	Maximum value of the tonic driver curve
MAX-Phasic	Maximum value of the phasic tonic curve
AUC-Tonic	Area under the tonic driver curve over time
AUC-Phasic	Area under the phasic driver curve over time
Mean-Tonic	Mean value of the tonic driver component
Mean-Phasic	Mean value of the phasic driver component
STD-Tonic	Standard deviation of the tonic driver component
STD-Phasic	Standard deviation of the phasic driver component

having a signal with a zero baseline peaks as distinguishable as possible. More details can be again found in [28].

C. Feature Extraction

Features were extracted from the $\text{DRIVER}_{\text{tonic}}$ and $\text{DRIVER}_{\text{phasic}}$ signals also studying the different effects of the IAPS and TAT elicitation. Features extracted from the $\text{DRIVER}_{\text{phasic}}$ signal were calculated into nonoverlapped time windows of 5 s, according to the knowledge that SCRs arise within 5 s after the stimulus onset [36], [37]. Nonoverlapped time windows are justified by the fact that the deconvolution algorithm misses overlapped responses lasting 4 s [28]. Therefore, despite the fact that IAPS stimuli were presented each 2 s, a sort of refractory period at least equal to 4 s is assumed for computational reasons. Features extracted from the $\text{DRIVER}_{\text{tonic}}$ component, instead, were calculated within nonoverlapped time windows of 20 s, the upper cutoff frequency of the tonic component being about 0.05 Hz [38]. Afterwards, features belonging either to IAPS or TAT elicitation were grouped accordingly. In Table II, the features set is summarized along with the corresponding description. Each feature was normalized by subtracting its correspondent value at rest.

Statistical analysis: Both the IAPS-related features and the TAT-related features extracted from several acquisitions were compared by using statistical analysis. The statistical inference analysis was performed by means of nonparametric tests due to the nonGaussianity of the samples ($p < 0.05$ given by the Kolmogor–Smirnov test with null hypothesis of Gaussian distributed samples). For each of the seven subjects (i.e., Pz01, Pz02, Pz04, Pz07, Pz08, Pz09, and Pz10) who performed the experiment twice, an intrasubject statistical analysis was performed. Each pair of acquisitions was compared by using a Wilcoxon test for paired data [39]. Moreover, an inter-subject analysis was performed in order to compare the acquisitions associated to the same mood label. In this case, different mood states (i.e., depression, mixed-state, and euthymia) were compared by means of a Kruskal–Wallis test to evaluate whether they statistically belonged to the same population. In case of rejection of the null hypothesis, the Mann–Whitney test for unpaired data [40] with a Bonferroni adjustment for every pair was carried out.

III. EXPERIMENTAL RESULTS

In this section, the experimental results performed on both groups of healthy subjects and bipolar patients are shown in detail. Further statistical analyses pointing out differences between the IAPS and TAT sessions, for each EDA feature and for each acquisition, as well as results on intra and intersubject evaluations are given below.

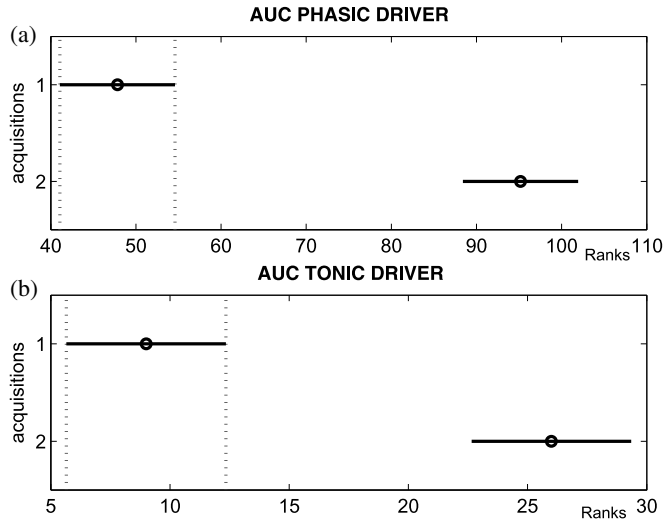

Fig. 4. Pz01's statistical analysis for IAPS elicitation. Results of Pz01's area under the curve (AUC) of (a) $\text{DRIVER}_{\text{phasic}}$ and (b) $\text{DRIVER}_{\text{tonic}}$ features.

Of note, the time constants τ_1 and τ_2 were independently estimated for each patient and for each healthy subject. Here, we report the following statistics calculated among all the 17 EDA series gathered from the ten bipolar patients: Median$\{$on $\tau_1 = 0.81$, on $\tau_2 = 2.49\}$, Median Absolute Deviation$\{$on $\tau_1 = 0.16$, on $\tau_2 = 0.79\}$, Min$\{$ on $\tau_1 = 0.49$, on $\tau_2 = 1.54\}$, and Max$\{$ on $\tau_1 = 1.24$, on $\tau_2 = 3.83\}$.

A. Study on Bipolar Patients

A summary of the clinical evaluations of the patients recruited for this study, expressed as mood label, is shown in Table I.

For each acquisition, we first performed a statistical analysis to test the null hypothesis of having no significant difference between the two affective elicitation sessions (i.e., IAPS and TAT sessions). As the samples were comprised of several values for each IAPS and TAT session (each feature value was computed within a sliding window), and a perfect temporal match between each sample cannot be ensured, the Mann–Whitney tests were used to compute the p-values. For each acquisition, we found significant differences ($p < 0.03$) for all of the considered EDA features but the STD-Tonic.

1) IAPS Stimulation: Wilcoxon test for paired data was applied on patients with two acquisitions, i.e., Pz01, Pz02, Pz04, Pz07, Pz08, Pz09, and Pz10. Statistical analysis results show that all the phasic features resulted to be statistically different for all subjects. Patients Pz02 and Pz04 showed a nonsignificant tonic features set between the two acquisitions. More in detail, patients Pz01, Pz07, Pz08, Pz09, and Pz10 exhibited significant increase in the mean value, in the area under the curve and in the maximum value of both $\text{DRIVER}_{\text{phasic}}$ and $\text{DRIVER}_{\text{tonic}}$ components during second acquisition (see an example in Fig. 4). Pz02 showed no statistical difference in tonic features, but an

TABLE III
RESULTS FROM THE BIPOLAR PATIENTS DATASET EXPRESSED AS STATISTICAL SIGNIFICANCE FOR EACH EDA FEATURE

IAPS	Pz01	Pz02	Pz04	Pz07	Pz08	Pz09	Pz10
MAX-Tonic	$\mathbf{< 10^{-6}}$	> 0.05	> 0.05	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$
MAX-Phasic	$\mathbf{< 10^{-4}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$
AUC-Tonic	$\mathbf{< 10^{-6}}$	> 0.05	> 0.05	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$
AUC-Phasic	$\mathbf{< 10^{-4}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 0.05}$	$\mathbf{< 10^{-6}}$
Mean-Tonic	$\mathbf{< 10^{-5}}$	> 0.05	> 0.05	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$
Mean-Phasic	$\mathbf{< 10^{-4}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 0.05}$	$\mathbf{< 10^{-6}}$
STD-Tonic	$\mathbf{< 0.05}$	> 0.05	> 0.05	> 0.05	> 0.05	$\mathbf{< 0.005}$	$\mathbf{< 10^{-4}}$
STD-Phasic	$\mathbf{< 10^{-4}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-4}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$

Samples are estimated during IAPS elicitation sessions of the two acquisition/mood states. p-values are from the Wilcoxon test.

TABLE IV
RESULTS FROM THE BIPOLAR PATIENTS DATASET EXPRESSED AS STATISTICAL SIGNIFICANCE FOR EACH EDA FEATURE

TAT	Pz01	Pz02	Pz04	Pz07	Pz08	Pz09	Pz10
MAX-Tonic	> 0.05	$\mathbf{< 0.05}$	> 0.05	> 0.05	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$
MAX-Phasic	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
AUC-Tonic	> 0.05	$\mathbf{< 0.01}$	> 0.05	> 0.05	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$
AUC-Phasic	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
Mean-Tonic	> 0.05	$\mathbf{< 0.01}$	> 0.05	> 0.05	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$	$\mathbf{< 10^{-6}}$
Mean-Phasic	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
STD-Tonic	> 0.05	$\mathbf{< 0.05}$	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
STD-Phasic	$\mathbf{< 0.005}$	> 0.05	> 0.05	$\mathbf{< 10^{-4}}$	> 0.05	> 0.05	> 0.05

Samples are estimated during TAT elicitation sessions of the two acquisition/mood states. p-values are from the Wilcoxon test.

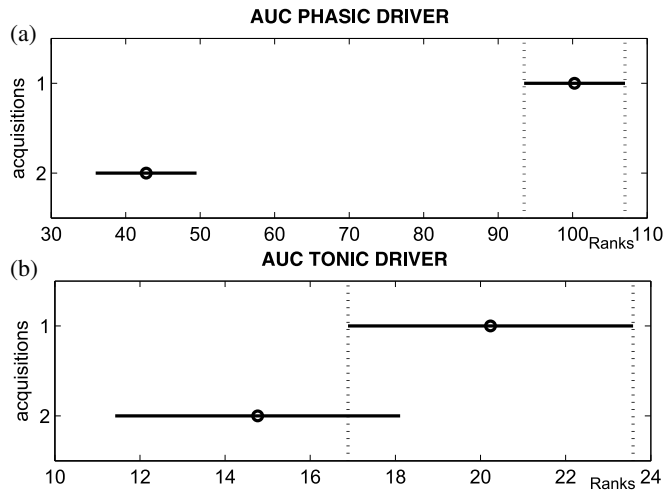

Fig. 5. Pz04's statistical analysis for IAPS elicitation. Results of Pz04's AUC of (a) $\mathrm{DRIVER}_{\mathrm{phasic}}$ and (b) $\mathrm{DRIVER}_{\mathrm{tonic}}$ features.

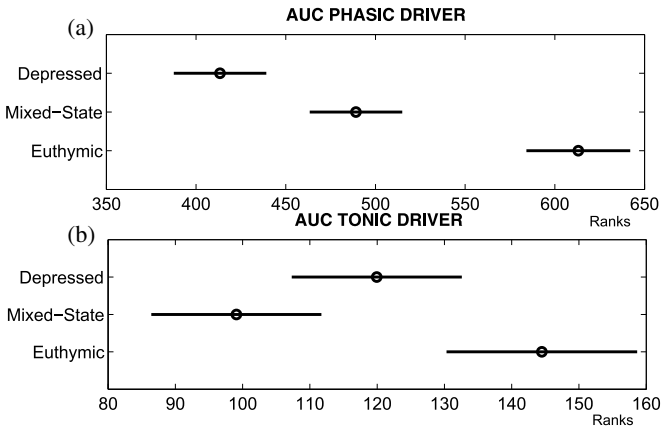

Fig. 6. IAPS stimulation: Intersubject statistical analysis. AUC of (a) $\mathrm{DRIVER}_{\mathrm{phasic}}$ and (b) $\mathrm{DRIVER}_{\mathrm{tonic}}$ features.

increasing significant trend of the phasic features was found. As all of five patients clinically improved (i.e., change into an euthymic state) their status, this results could be due to an increased sympathetic activity during the emotional stimulation session [18]. On the contrary, Pz04 showed a significant decrease for all phasic features in the second acquisition as compared to the first one, whereas tonic features were not statistically different (see an example in Fig. 5). Yet, this result can be interpreted as a reduction of sympathetic activity when moving from a mixed state, where hypomanic symptoms could be present, to an euthymic condition [18]. The standard deviation of both $\mathrm{DRIVER}_{\mathrm{tonic}}$ and $\mathrm{DRIVER}_{\mathrm{phasic}}$ components showed a similar trend between the two acquisitions for all of the seven patients having two observations. In particular, STD-Tonic and STD-Phasic decreased in the second acquisition, i.e., euthymic state.

Furthermore, an intersubject statistical analysis was performed including also the patients with one acquisition only. Data were not considered as coming from a specific subject but grouped following clinical classification. A Kruskal–Wallis test was carried out among acquisitions classified as depressed, mixed-state, and euthymic. The mean value and AUC of the $\mathrm{DRIVER}_{\mathrm{phasic}}$ signal significantly discriminated the three mood states ($p < 10^{-6}$). In particular, these two features exhibited the same trend, i.e., they increase from depression to euthymia through mixed-state [see Fig. 6(a)]. The maximum value of $\mathrm{DRIVER}_{\mathrm{phasic}}$ was able to distinguish the depressed mood states from the group mixed-state plus euthymic state ($p < 10^{-6}$). Instead, the mixed-state and the euthymic state did not show a significative difference ($p > 0.05$).

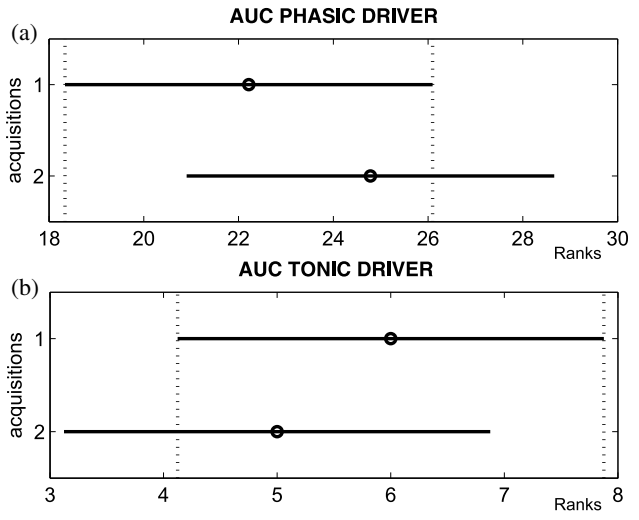

Fig. 7. Pz01's statistical analysis for TAT elicitation. Results of Pz01's AUC of (a) $\mathrm{DRIVER}_{\mathrm{phasic}}$ and (b) $\mathrm{DRIVER}_{\mathrm{tonic}}$ features.

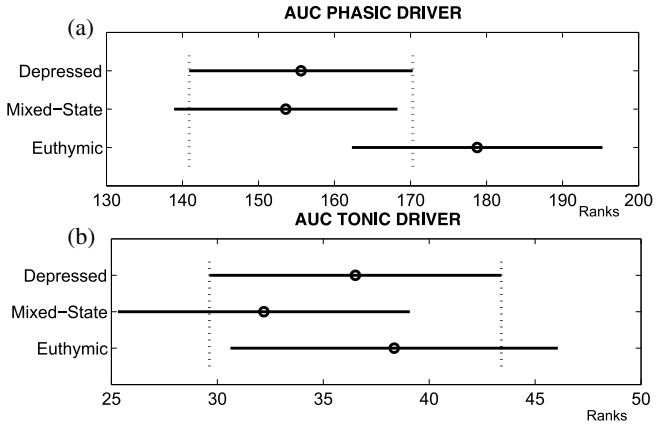

Fig. 8. TAT stimulation: Intersubject statistical analysis. AUC of (a) $\mathrm{DRIVER}_{\mathrm{phasic}}$ and (b) $\mathrm{DRIVER}_{\mathrm{tonic}}$ features.

Concerning features extracted from $\mathrm{DRIVER}_{\mathrm{tonic}}$ [see Fig. 6(b)], the Kruskal–Wallis test showed significant differences among the three different mood states ($p < 10^{-6}$), despite the fact that the depression and mixed-state group and the depression and euthymic group did not show a significant difference ($p > 0.8$).

2) TAT Stimulation: Likewise, the analysis was performed on signals gathered from the IAPS stimulation, statistical analyses were performed considering intra and intersubject evaluations. Concerning the intrasubject analysis, features extracted from $\mathrm{DRIVER}_{\mathrm{phasic}}$ data of patients who underwent two acquisitions showed no significant difference between the two acquisitions (see Fig. 7) except for the standard deviation of the $\mathrm{DRIVER}_{\mathrm{phasic}}$ of Pz01 and Pz04. Instead, features extracted from the $\mathrm{DRIVER}_{\mathrm{tonic}}$ data showed significant differences between the two acquisitions of Pz02, Pz08, Pz09, and Pz10.

Moreover, the intersubject statistical analysis was performed by means of a Kruskal–Wallis test among acquisitions classified as mixed-state, depressed, and euthymic, considering also the patients with only one acquisition. The results [see Fig. 8(b)] demonstrated that features extracted from both $\mathrm{DRIVER}_{\mathrm{tonic}}$ and $\mathrm{DRIVER}_{\mathrm{phasic}}$ showed no significant differences among mood states ($p > 0.05$).

B. Control Subjects

We performed statistical analyses based on the Wilcoxon test for paired samples to investigate whether differences on the EDA feature patterns of healthy subjects are statistically significant between multiple affective elicitation protocols over time. Likewise, the analysis performed on the bipolar patient group, the features reported in Table II were extracted from both the $\mathrm{DRIVER}_{\mathrm{phasic}}$ and $\mathrm{DRIVER}_{\mathrm{tonic}}$ series. We report that the intersubject statistical analysis independently performed considering the data from the IAPS and TAT sessions showed no statistically significant differences between the two acquisitions on each of the considered EDA features ($p > 0.05$).

IV. Discussion and Conclusion

In this study, EDA analysis was performed in ten bipolar patients recruited in the frame of the European project PSYCHE [10], [14], [29]. Each patient's mood state was clinically evaluated as depressed, euthymic, or mixed. The patients were asked to passively view a set of IAPS images and to describe TAT pictures. Novelties of this study are mainly related to data, experimental protocol, and signal processing methodology. Comparative analyses on different emotional elicitations, in fact, have never been considered in studying mental disorders such as bipolar disorders, especially in patients experiencing mixed-state symptoms. Moreover, the innovative application of the EDA analysis through deconvolutive model allowed us to effectively test the experimental hypothesis of having different sympathetic activations among different pathological mental states. As a consequence, the proposed EDA feature set could have a prognostic value on mental illness and can be evaluated when the SMNA is estimated using a deconvolution model. A deconvolution analysis was applied to the EDA signals in order to perform an effective separation of the EDA components into tonic and phasic drivers. Several features were extracted in order to quantify and characterize such components allowing for intra and intersubject statistical analysis. On the basis of the obtained results, we can formulate different conjectures. As the IAPS stimulation provoked consistent changes in all of the features of the phasic components, and with the phasic signals being strongly stimulus-related, we can conclude that the IAPS pictures elicited a much stronger emotional response than the TAT stimuli. As a matter of fact, significant statistical differences were found in the whole EDA feature pattern between the IAPS and TAT elicitation sessions. Moreover, the idea behind this study is that when a patient is depressed, he/she reacts less intensively to high arousing stimuli than while in mixed-state, while sympathetic activity remarkably increases when the patient is in the euthymic state. This is confirmed by Fig. 6(a). Accordingly, Table V shows how the phasic contribution increases or decreases during mood swings. The discordant trend of Pz04 can be justified by the presence in the mixed-state of maniac symptoms, even if the literature is quite poor on the

TABLE V
SPECIFICATION OF INCREASING OR DECREASING TRENDS OF EDA PHASIC COMPONENTS DURING CLINICAL MOOD SWINGS

	Pz01	Pz02	Pz04	Pz07	Pz08	Pz09	Pz10
	Depressed Euthymic	Depressed Euthymic	Mixed-state Euthymic	Depressed Euthymic	Mixed-state Euthymic	Mixed-state Euthymic	Depressed Euthymic
MAX-Phasic	↑	↑	↓	↑	↑	↑	↑
AUC-Phasic	↑	↑	↓	↑	↑	↑	↑
Mean-Phasic	↑	↑	↓	↑	↑	↑	↑

Up-arrow and down-arrow intend an activity increase and decrease between the two acquisitions, respectively.

relationship between maniac states and EDA. Analysis of features extracted from the tonic signal (stimulus-unrelated component) during the IAPS stimulation revealed a significant difference in the acquisitions of all the patients except Pz02 and Pz04. As a consequence, on the basis of the limits of the results, no final conclusion can be drawn about a possible link of this component and mood swings. TAT is meant to reveal underlying motives as well as the manner in which people interpret social situations. In this task, only a few significant changes in the tonic EDA were found over the different acquisitions. Features extracted from phasic drivers did not differ significantly over mood swings. Statistical analyses were also intended as intersubject evaluations and performed using the KruskalWallis nonparametric test. Accordingly, post-hoc analysis engaged nonparametric Mann–Whitney tests considering the Bonferroni adjustment of the statistical significance. Grouping the acquisition with the same label, the statistical analysis showed strong differences among the three mood states under examination. Specifically, for IAPS elicitation, phasic features well discriminated among depression, mixed state, and euthymia. An incremental trend of the signal was observed over these three states. The depression condition is confirmed to lead to a severe decrease of the electrodermal response activity and, consequently, of the ANS activity. During the mixed-state phase, the patients exhibit a higher level in the phasic activity, i.e., a stronger response to the stimuli, which is, however, significantly lower than that seen in the euthymic state, in which the subject feels like in normal conditions.

Differently, the tonic features regarding IAPS stimuli showed a strong separation between the euthymic and mixed-state, which shows a strong tonic hypoactivity. The tonic component, which is not directly connected to the stimuli but is related to the state of the subject, showed an overlap between the depressive and mixed-state and the depressive and euthymia. TAT stimuli did not reveal any statistical differences among the three mood states both for the tonic and phasic features. Therefore, TAT was not able to elicit changes in the ANS activity of a bipolar patient. This result can be due to the fact that pictures from TAT were not as emotionally arousing as the IAPS pictures.

Finally, results performed on healthy subjects strongly support the hypothesis that the EDA signal processing provides a viable decision support system for mental disorders. Healthy subjects, in fact, showed no statistical difference on each of the EDA feature pattern between multiple affective elicitation along the time. Thus, it is reasonable that the coherent changes found in the bipolar patients group can be considered as real biomarkers of pathological mood states. Tables VI summarize the results gathered from all of the patients and healthy subjects. Values of each elicitation session are normalized with respect to the baseline ones and expressed as the intersubject 95% confidence interval.

TABLE VI
95% CONFIDENCE INTERVALS FOR THE EDA FEATURES IN HEALTHY SUBJECTS AND BIPOLAR PATIENTS AMONG DIFFERENT MOOD STATES

AUC-Phasic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	60.47 ± 0.323	37.21 ± 1.44
	Depression	55.01 ± 0.55	36.18 ± 1.94
	Mixed State	59.01 ± 0.65	34.21 ± 3.68
Healthy Subjects		64.58 ± 0.81	97.28 ± 0.1

Mean-Phasic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	0.19 ± 0.0013	0.15 ± 0.006
	Depression	0.12 ± 0.0020	0.14 ± 0.027
	Mixed State	0.13 ± 0.0021	0.13 ± 0.008
Healthy Subjects		0.48 ± 0.0017	0.52 ± 0.0023

MAX-Phasic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	0.25 ± 0.0021	0.16 ± 0.0084
	Depression	0.22 ± 0.0023	0.12 ± 0.03
	Mixed State	0.24 ± 0.0024	0.17 ± 0.0051
Healthy Subjects		0.69 ± 0.0024	0.73 ± 0.0029

AUC-Tonic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	1068.11 ± 48.16	128.06 ± 14.6
	Depression	1008.47 ± 56.25	118.42 ± 15.8
	Mixed State	891.60 ± 23.27	108.51 ± 12.6
Healthy Subjects		15.7 ± 1.02	24.10 ± 1.61

Std-Phasic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	0.0026 ± 0.00027	0.018 ± 0.002
	Depression	0.004 ± 0.00036	0.021 ± 0.0023
	Mixed State	0.0013 ± 0.00032	0.012 ± 0.0016
Healthy Subjects		0.13 ± 0.0003	0.13 ± 0.0004

MAX-Tonic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	1.05 ± 0.05	0.043 ± 0.02
	Depression	0.99 ± 0.04	0.51 ± 0.07
	Mixed State	0.86 ± 0.028	0.43 ± 0.048
Healthy Subjects		1.53 ± 0.073	1.72 ± 0.071

Mean-Tonic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	1.06 ± 0.048	0.43 ± 0.018
	Depression	1.01 ± 0.06	0.51 ± 0.063
	Mixed State	0.89 ± 0.023	0.43 ± 0.051
Healthy Subjects		1.39 ± 0.073	1.51 ± 0.072

Std-Tonic	Mood	IAPS	TAT
Bipolar Patients	Euthymia	0.01 ± 0.0011	0.0032 ± 0.0008
	Depression	0.014 ± 0.0022	0.0051 ± 0.0009
	Mixed State	0.007 ± 0.0012	0.0022 ± 0.0005
Healthy Subjects		0.12 ± 0.0007	0.13 ± 0.0006

Normalized IAPS and TAT values through baseline value subtraction.

In conclusion, our results confirm the hypothesis of a link between changes in the EDA and mood states. Specifically, EDA strongly changed in the different mood states in response to affective stimuli, showing a specific decrease in depressive phases. On this basis, we conclude that EDA variations in phasic components may be suitable markers for discriminating mood states

in bipolar patients. Future methodological works can be related to the definition of novel features and, especially, a patient-specific threshold used for the identification of the EDA tonic and phasic drivers. Moreover, experimental protocols involving comfortable wearable EDA monitoring systems such as sensorized textile-based gloves [41], [42] can be taken into account in order to study EDA dynamics also in a naturalistic environment, may be along with other ANS signs (e.g., eye-gaze and pupil size variation [43]).

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