

Lateralized electrodermal dysfunction and complexity in patients with schizophrenia and depression

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Abstract

OBJECTIVE: Recent evidence indicates that in psychiatric patients with schizophrenia and depression, lateralized EDA changes linked to temporal-limbic electrophysiological dysfunction occur. These clinical findings provide evidence for brain asymmetry and disruptions related to integrative brain activity in pathological conditions.

METHODS: These changes in brain asymmetry may be assessed by linear analysis of EDA measurement and nonlinear analysis of brain complexity calculated as information entropy. Two groups of patients with established diagnosis of paranoid schizophrenia (N=35), unipolar depression (N=35) and a control group of 35 healthy controls were examined by measurement of bilateral electrodermal activity (EDA). In non-linear data analysis of the EDA time series in resting state the method of recurrence quantification analysis was applied.

RESULTS: In these patients significant right–left EDA asymmetry and asymmetry of information entropy calculated by non-linear recurrence quantification analysis of EDA records have been found. Similar asymmetry has not been observed in the group of healthy controls.

CONCLUSIONS: Because information entropy reflects the complexity of the deterministic structure in the system, then unilaterally increased entropy in patients with schizophrenia and depression likely indicates specific nonlinear disturbances in limbic circuits that modulate EDA. These data are in accordance with recent findings that indicate apparent differences in nonlinear neural patterns in the psychiatric diseases and nonlinear behavior of healthy brain.

Introduction

Electrodermal activity (EDA) has been described as a sensitive electrophysiological measure of limbic modulation influences and correlates with amygdala activity although other structures such as ventromedial and dorsolateral prefrontal cortices, anterior cingulate gyrus, parietal lobe, insula and hippocampus in EDA modulation are also involved [9,26,27]. Evidence for the role of the amygdala in the expression of EDA mainly comes from functional imaging studies [9,19] and lesion studies [1,2,7,8]. EDA typically reflects activity within the sympathetic axis of the autonomic nervous system. Sympathetic activity is closely linked to emotion and EDA is widely used as a sensitive index of emotion-related sympathetic activity [6,9,11,18,30]. This coupling enables to use EDA as an objective index of emotional behavior or an indicator of conditioning in humans [9]. According to EDA measurements in psychiatric patients with schizophrenia and depression, lateralized EDA changes linked to temporal-limbic electrophysiological dysfunction has been found [23,24]. These data indicate that unilateral electrophysiological dysfunction related to overactivation and left–right asymmetry predominantly occurs on the left in schizophrenia and on the right in depression [16,21,22,24]. In schizophrenia neuroanatomical asymmetries are known to be present in the brain, particularly through changes in the left temporal lobe. In addition to disturbed neuroanatomical asymmetries, disturbed neurochemical asymmetries have also been reported in the brains of patients with schizophrenia. These changes in normal asymmetry of the temporal lobe in schizophrenia might be due to a disruption of the neurodevelopmental processes involved in hemispheric lateralization [28]. Also in depression experimental data using transcranial magnetic stimulation confirm a slightly lower activation in the left hemisphere than in the right in depressive syndromes [20]. These clinical findings provide evidence for discussion of the significance of unbalanced hemispheric activation and related disruptions of integrative brain activity as a biological substrate of affective disorders and schizophrenia [12,15,20]. These findings are based on the complexity theory focused on the study of brain spatio-temporal structure. The spatio-temporal structure in pathological brain states may be more regular which display excessive order with lower complexity than normal or more irregular as uncorrelated randomness with higher complexity. The states of periods of high complexity are characterized by activity of independent areas related to fast parallel information processing that runs in a distributed mode. It means that numerous processes from sensory and cognitive channels are executed simultaneously and this desynchronized neural state may be related to active information processing in the cortex [29]. Together these findings suggest the hypothesis that dynamic changes in EDA complexity, indicating nonlinearities of limbic modulation influences as measured by EDA are present in the patients with schizophrenia and

depression. The aim of the present study is to investigate the relationship between linear and non-linear activities in EDA by examining of the linear EDA asymmetry and the information entropy as a non-linear measure of complexity in the schizophrenic patients, depressive patients and normal controls.

Methods

Participants

The participants consisted of 35 adult schizophrenic outpatients, 35 depressive inpatients (from the university hospital) and 35 healthy controls from general population. The 19 males and 16 females from schizophrenia group (mean age of 28.2), 13 males and 22 females from depressive group (mean age of 43.4) and the 15 males and 20 females from healthy controls group (mean age of 23.7) took part in the study. Schizophrenic patients had diagnosis of paranoid schizophrenia and depressed patients had diagnosis of unipolar depression (recurrent depression or depressive period). All the schizophrenia patients were in partial remission. Their treatment at the time of the recruitment was based on antipsychotic medication. Treatment status of the depressive patients was in partial remission without psychotic symptoms and their treatment was based on antidepressant medication. Exclusion criteria were any form of epilepsy, organic illnesses involving the central nervous system, substance, and/or alcohol abuse, mental retardation and significant extra-pyramidal symptomatology. All the participants were strongly right handed according to Waterloo Handedness Questionnaire [14].

Design

The clinical study assessed 35 adult patients with diagnosis of paranoid schizophrenia, 35 adult patients with diagnosis of depression and 35 healthy controls. In the assessment measurement of bilateral electrodermal activity in the patients and healthy controls were used. Investigations took place in a quiet room at the temperature 23 °C with informed consent of all the participants.

Measures

Electrodermal measurement

After obtaining informed consent from the participant, the EDA was recorded bilaterally using two channels SAM unit and Psylab software (Contact Precision Instruments) connected to personal computer. Measurement was performed in a quiet room, with room temperature of about 23 °C. The participant was instructed to sit down into comfortable chair. Then two pairs of Ag/AgCl electrodes (8 mm diameter active area) filled with electro-conductive-paste were attached to medial phalanges of the index and middle finger of each hand. After five minutes relaxation with closed eyes experimental EDA recording began and took a time of two minutes.

Data analysis

Descriptive statistics in a statistical evaluation included medians, means and standard deviations. For further statistical evaluation, t-tests for independent samples for the groups of patients and normal healthy controls were calculated.

Non-linear data analysis of the EDA time series in relaxed state was performed using the method of recurrence quantification analysis and software package Visual Recurrence Analysis which is a well-known software for the time series analysis and is especially suitable for analysis of non-stationary nonlinear processes. EDA records were divided on 8 second intervals (which include 8000 datapoints) and then nonlinear analysis was performed. In the data analysis by common technique mutual information, False Nearest Neighbours, embedding dimension and information entropy were calculated [25]. False Nearest Neighbours technique utilizes geometric principles for the finding of embedding dimension and further indicators of non-linear dynamics such as information entropy [25] that reflects the complexity of the deterministic structure in the system. A form of visualization of dynamic changes and recurrence states enables recurrence plots and quantification of this dynamic relationships embodied in recurrence plots enables the method called recurrence quantification analysis a method introduced by Eckmann [13].

Results

Results of EDA indicate significant hyperarousal in the patients with paranoid schizophrenia and significant hypoarousal in the patients with depression with respect to healthy controls (Table 1). EDA results also indicate significant bilateral asymmetry in the patients with respect to healthy controls. Similar asymmetry has been also found for information entropy obtained by recurrence quantification analysis. The entropy reflects the complexity of the deterministic structure of the system and unbalanced hemispheric activation (Table 1). Visible differences in EDA related hemispheric asymmetry have also been observed in results of visual recurrence analysis by visual comparison of recurrence plots. Examples of visible differences for the patients and only small differ-

ences in healthy control are in Figure 1. As a result the data indicate that significant linear asymmetry observed in EDA measurement in schizophrenia and depression is related to nonlinear changes calculated by nonlinear data analysis from recurrence plots which indicate laterality related disruptions in brain complexity.

Discussion

Several recent findings including results of this study indicate that unilateral electrophysiological dysfunction predominantly occurs on the left in schizophrenia and on the right in depression [24]. Results of EDA indicate significant hyperarousal in the patients with paranoid schizophrenia and significant hypoarousal in the patients with depression with respect to healthy controls. These findings are in accordance with EDA findings recorded from the left and right hands in unilateral temporal lobectomy patients which provide evidence for a state of hypoarousal in right temporal patients and some support for hyperarousability in lefts [10]. Similar findings have also been reported in temporal lobe epilepsy patients with left or right temporal foci who had schizophrenia or depression as psychiatric comorbidity. These epileptic patients had electrophysiological dysfunction, predominantly on the left in the case of schizophrenia and on the right in depression [16,17]. These findings indicate the relationship between temporal-limbic dysfunction measured by EDA and bilateral asymmetry for information entropy calculated from EDA records in the schizophrenic and depressive patients with respect to healthy controls. Because information entropy reflects the complexity of the deterministic structure of the system it is probable to suppose that unilaterally increased complexity is linked to unbalanced hemispheric activation and related disruptions of integrative brain activity as a neural substrate of affective disorders and schizophrenia. Because high complexity characteristic for activity of independent areas and fast parallel information processing in a distributed mode are characteristic for epileptiform events in the brain, the brain entropy may also indicate characteristic changes that lead to epileptiform activity as an important factor in psychiatric disorders [3,4,5]. These changes related to epileptiform activity may cause

Table 1. Descriptive statistics of EDA and information entropy for the schizophrenic patients, depressive patients and for the healthy controls.

	MeanEDA L	MeanEDA R	MeanEntr. L	MeanEntr. R	L-R t-test EDA	L-R t-test Entr.
Schizophrenia	7.08±5.9	2.87±2.10	5.18±0.55	4.82±0.51	T=3.92; p=0.0002	3.27; p=0.0015
Depression.	1.61±1.31	2.56±2.28	4.73±0.43	4.97±0.52	T= -2.33; p=0.022	-2.63; p=0.0097
Controls	2.91±1.51	2.79±1.26	4.84±0.395	4.86±0.38	T=0.37; p=0.71	-0.288; p=0.773

EDA= electrodermal activity (micro-Siemens); Entr.= Information Entropy (bits)

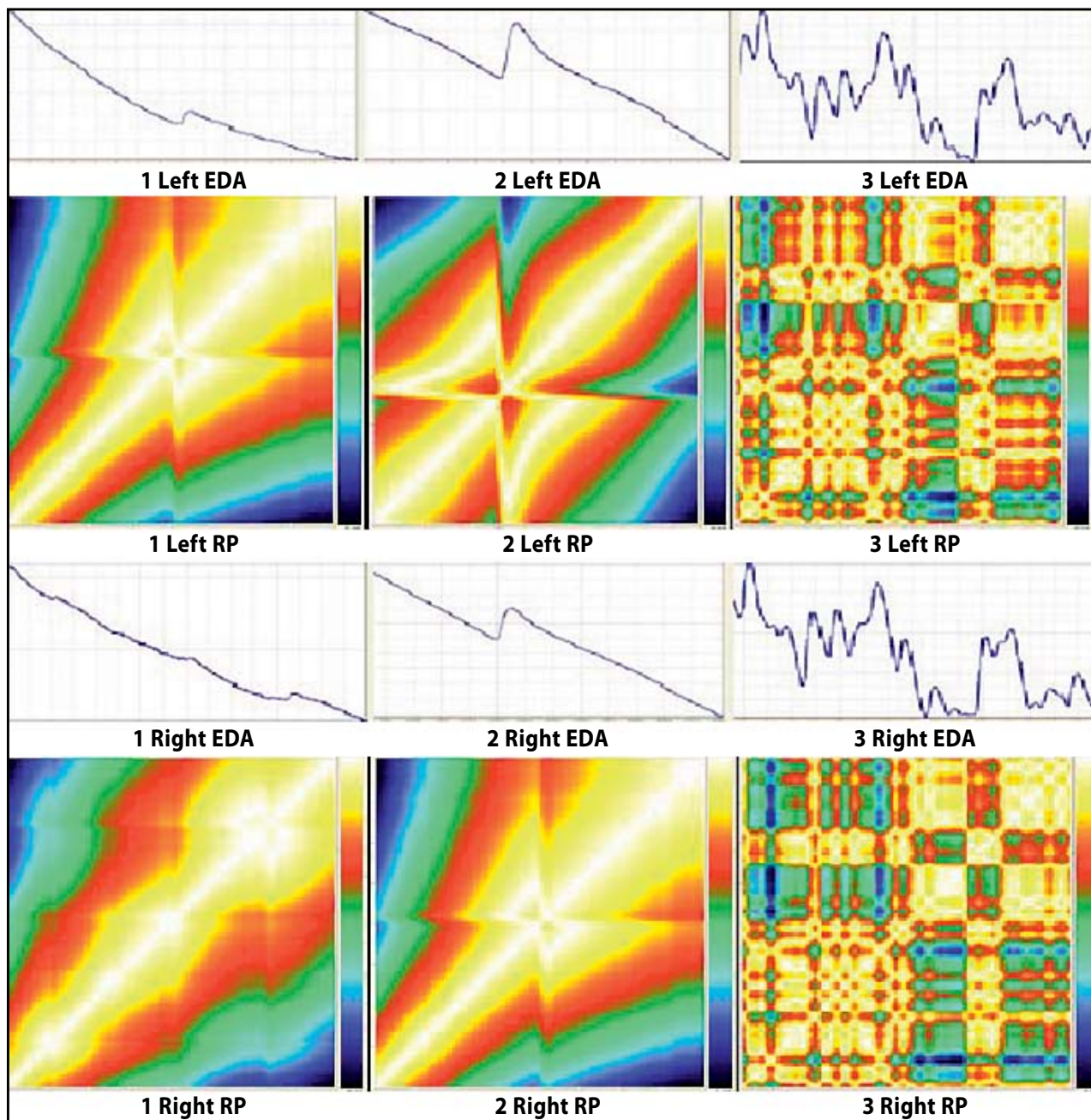


Figure 1. Examples of EDA charts and recurrence plots (RP) displaying Left-Right asymmetry: 1) schizophrenic patient Mean Entr. (in bits) (L=5.89;R=4.53); 2) depressive patient Mean Entr. (L=4.41;R=5.93); 3) normal control individual Mean Entr. (L=5.2;R=5.32)

the specific characteristics of unbalanced hemispheric interaction in schizophrenia and depression. Future perspective of nonlinear analysis of EDA from this point of view may be identification of patients with the specific dynamic abnormalities who might be well indicated for anticonvulsant therapy. Further research may well determine whether the methods of non-linear recurrence quantification and visual recurrence analysis are able to provide a clearer understanding of these processes and serve in the future as a useful practical instrument for diagnostics and therapy of these mental disorders.

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