Advs Exp. Medicine, Biology - Neuroscience and Respiration (2016) 26: 83–88
DOI 10.1007/5584_2016_40

Published online: 23 June 2016

Electrodermal Activity in Adolescent Depression

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Abstract

Major depressive disorder (MDD) is characterized by dysphoric mood, which may be accompanied by suicidal ideation. It is supposed that MDD is associated with dysfunction of the autonomic nervous system, but studies in pediatric patients are rare. Therefore, we aimed to study the relationship between MDD and autonomic regulation in adolescence using the electrodermal activity as an index of sympathetic cholinergic control. We examined 25 adolescents suffering from MDD without comorbidities and prior to pharmacotherapy (13 girls, mean age 14.6 ± 0.4 year) and 25 age/gender-matched healthy control subjects. The electrodermal activity was continuously recorded during 5 min of supine rest. The value of this activity in μS was averaged for each minute of the recording. We found that in depressed patients, electrodermal activity was significantly lower each minute of the recording compared to that in the control group. The study demonstrates electrodermal hypoactivity in adolescent patients with MDD, which points to dysfunctional regulation of the sympathetic part of the autonomic nervous system. This finding could represent a potential pathomechanism leading to higher risk of negative health outcomes in pediatric depressed patients. Further research is needed to elucidate the incompletely understood interaction between MDD and autonomic regulatory outputs at young age.

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Keywords
Autonomic nervous system • Cardiovascular risk • Major depressive disorder • Pediatric patients • Sympathetic activity

1 Introduction

Major depressive disorder (MDD) is a mental disorder characterized by psychological symptoms, e.g., dysphoric or irritable mood, feelings of worthlessness, and thoughts of death, including suicidal ideation (APA 2013). It is supposed that MDD is associated with dysfunction of the autonomic nervous system, which represents a key regulatory system for the maintenance of homeostasis, adaptability, and physiological flexibility of the organism. For instance, impaired sympathetic function is probably one of the mechanisms involved in increased cardiovascular risk associated with MDD (Carney and Freedland 2009). Therefore, detailed study of the relationship between MDD and dysregulation of the autonomic nervous system could bring novel important information about pathomechanisms of depression-related negative health outcomes.

There are only a few noninvasive methods for the assessment of sympathetic function. One of the suitable markers reflecting sympathetic regulation is electrodermal activity (EDA). EDA is represented by skin conductance that depends on the amount of sweat produced by eccrine sweat glands. When the sweat duct is filled with sweat, more conductive area originates on the nonconductive corneu (Cacioppo et al. 2007). While the sweat glands are innervated by sympathetic fibers, their synaptic neurotransmission is mediated almost exclusively by acetylcholine. Thus, EDA provides a direct representation of solely sympathetic cholinergic activity in contrast to the majority of systems regulated by the two main branches of the autonomic nervous system (Fowles 1980).

EDA is accepted as a noninvasive marker of sympathetic arousal in psychophysiological research (Jacobs et al. 1994). It has become a frequently used tool in the research on mental disorders, including MDD. Interestingly, many studies in the last decades have shown that depressed patients have a lower EDA compared with controls (Wolfersdorf et al. 1996; Williams et al. 1985; Ward et al. 1983; Dawson et al. 1977). These results led to the assumption that reduced EDA could be an important biopsychological trait in the etiology of depression. However, previous studies have evaluated EDA in adult depressed patients and studies at adolescent age are very rare (Crowell et al. 2012). Therefore, in the present study we set out to determine the baseline EDA in adolescent patients suffering from MDD, prior to pharmacological treatment.

2 Methods

The study was approved by the Ethics Committee of Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Slovakia and it comported with Declaration of Helsinki. All subjects and their parents were instructed about the study protocol and they gave written consent to participate at study entry.

2.1 Subjects

We examined 25 patients (F/M – 13/12) with MDD of the mean age of 14.4 ± 0.4 (range 11–17 years) and 25 gender- and age-matched healthy control subjects. The persons suffering from MDD were recruited from the inpatients admitted to a Psychiatric Clinic. The diagnosis of MDD, a single episode without psychotic symptoms (e.g., mood congruent or incongruent delusions, hallucinations) and other psychiatric disorders (e.g., ADHD, conduct disorders,

anxiety disorders), was classified by a thorough clinical investigation based on unstructured diagnostic interview conducted by a staff psychiatrist, specialized in child/adolescent disorders, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). The patients were examined before pharmacotherapy during the first week of hospitalization.

The exclusion criteria for both MDD and control group were: history of cardiovascular, respiratory, endocrinological, neurological, metabolic, or infectious diseases. The control subjects have never been treated for any mental disorder.

2.2 Study Protocol

All subjects were examined after breakfast in a quiet room under standard conditions (temperature: 22–23 °C, humidity: 45–55 %), with the minimization of stimuli, in the morning between 8:00 and 12:00 a.m. After 10 min of rest in the sitting position, the subject changed position into supine and remained at rest for further 5 min. Then, EDA was continuously recorded for another 5 min using a biofeedback device ProComp Infinity (Thought Technology Ltd., Canada). According to the general recommendations, sensors were placed on the medial phalanges of the second and the fourth finger of the non-dominant hand (Cacioppo et al. 2007).

2.3 Data Analysis

The recordings were visually checked and rare artifacts were removed manually. For a more accurate assessment of EDA changes, a 5-min recording time in the supine position was divided into five consecutive intervals of 60 s each. The mean value of EDA (in μS) was evaluated for each interval.

Data were expressed as means ± SE. The non-Gaussian/Gaussian distribution was ascertained by the Lilliefors test. The Mann-Whitney *U* test was used for between-groups comparison. A p-value of less than 0.05 defined the statistical significance of differences. Statistical analyses were performed using a commercial statistical package SYSTAT 10 for Windows (SSI, Richmond, CA).

3 Results

Recordings of electrodermal activity show that it was diminished in the supine resting position in adolescent patient with major depressive disorder compared with that in healthy subjects (Fig. 1a, b). A detailed analysis revealed that EDA was significantly lower in depressed patients, as compared with control subjects, during each minute interval of the 5-min recording time ($p < 0.01$; Table 1).

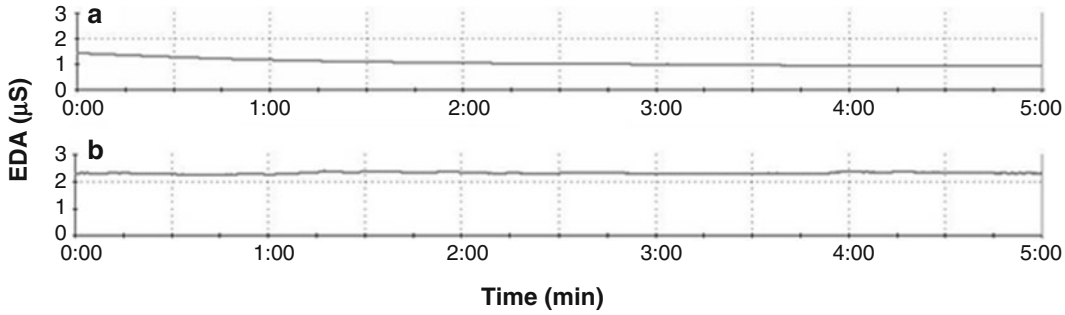

Fig. 1 Recordings of electrodermal activity (EDA) at rest in adolescents with major depressive disorder (**a**) and in healthy subjects (**b**). EDA – electrodermal activity

Table 1 Electrodermal activity (EDA), expressed in μS, in adolescents with major depressive disorder and healthy control subjects

Recording time (min)	Depressed (n = 25)	Healthy (n = 25)	p
1	1.46 ± 0.21	2.74 ± 0.33	p = 0.002
2	1.26 ± 0.19	2.52 ± 0.30	p = 0.001
3	1.22 ± 0.20	2.35 ± 0.29	p = 0.001
4	1.21 ± 0.20	2.20 ± 0.30	p = 0.004
5	1.18 ± 0.20	2.18 ± 0.29	p = 0.002

Data are means ± SE

4 Discussion

The major finding of this study was a significantly reduced EDA, indicating sympathetic hypoarousal, in depressed adolescents. Some previous studies have shown reduced EDA in adult depressed patients (Wolfersdorf et al. 1996; Williams et al. 1985; Ward et al. 1983), but others have reported no difference between depressed and healthy subjects (Toone et al. 1981). Nonetheless, there is a consistent impression that the majority of reports point to the presence of electrodermal hypoactivation in adult depressed patients (Miller 1995). We now extend and strengthen those findings by showing dampened electrodermal activity in depression of the adolescent age as well.

The mechanism of electrodermal hypoactivity remains debatable. It is well-known that EDA is determined by the integration of central and peripheral regulatory mechanisms. In the context of central regulation, complex interaction of cortical and subcortical structures forms three major systems: limbic-hypothalamic circuit, premotor cortex-basal ganglia system, and reticular formation. Thermoregulatory and emotionally driven limbic-hypothalamic system involves the excitatory effect of amygdala, the inhibitory role of hippocampus, and the intense connections with the ventromedial prefrontal cortex (vmPFC) (Boucsein 2012). Importantly, vmPFC is responsible for the EDA regulation during restful states in a manner that increased vmPFC activity is associated with decreased EDA. However, it is worth noting that vmPFC shows an internal functional heterogeneity and reduced EDA is predominantly caused by activation of its posterior region (Zhang et al. 2014). Further, vmPFC seems significantly involved in the pathomechanism of depression. The activity of the posterior part of vmPFC is related to a negative mood and it is enhanced in MDD patients. In contrast, activation of the anterior part of vmPFC is related to a positive mood, positively correlates with EDA, and it is decreased in MDD patients (Zhang et al. 2014; Myers-Schulz and Koenigs 2012). It is then a rational assumption that the present finding of reduced EDA in depressed adolescents could result from the imbalance between the activities of anterior and posterior regions of vmPFC. This assumption is in line with the contemporary neural models of depression which posit that dysfunction of medial prefrontal network and related limbic structures represents a key pathomechanism of emotional, behavioral, and other cognitive aspects of MDD. The rationale of this theory is based on the findings of distinct alterations in the gray matter volume, cellular elements, neurophysiological activity, receptor pharmacology, and gene expression in mood disordered subjects. The structures outlined above also exert a modulatory influence over the autonomic functions *via* connections with the hypothalamus and the brainstem, and thus are capable of altering the activity of peripheral organs, e.g., the cardiovascular system or sweat glands (Price and Drevets 2010). Yet this issue is still discussed and a straightforward effect of one brain area on the complex dynamic emotional and autonomic regulation is certainly too simplistic. The exact mechanisms underlying the function of the

prefrontal-limbic network in the MDD-linked autonomic dysregulation remain to be settled.

Another mechanism of electrodermal activity regulation could include the premotor cortex-basal ganglia system which partakes in setting specific motor actions (Boucsein 2012). The MDD is associated with variable abnormalities of behavioral systems (Kasch et al. 2002), which could be related to EDA (Fowles 1980). However, in the present study, recordings of EDA were performed under a resting condition, so that the influence on EDA of this neural circuit is rather unlikely.

Regarding peripheral regulation, it is generally accepted that human sweat glands have predominantly sympathetic cholinergic innervation from the sudomotor fibers originating in the sympathetic chain. It is assumed that depressed patients may have an abnormal peripheral cholinergic mediation, which could be represented by altered receptor sensitivity (Drevets et al. 2013; Miller 1995). Thus, the peripheral component also should be taken into account. In addition, function of the autonomic nervous system could be affected by pharmacotherapy. The effect of antidepressants has been considered as a possible pathomechanism of reduced EDA in MDD (Schnur 1990). Patients in the present study were examined prior to pharmacological treatment, and thus the influence on EDA of pharmacotherapy seems unlikely either.

In summary, reduced EDA in adolescents with MDD may result from a complex interaction of several pathomechanisms, some of which may still remain unknown. Importantly, altered autonomic regulation expressed by electrodermal hypoactivity is associated with increased risk of negative health outcomes, e.g., cardiovascular complications. Our previous studies of adolescent MDD have revealed impaired autonomic neurocardiac integrity, such as decreased vagal and increased sympathetic cardiac activity, and reduced complexity of the heart rate control (Tonhajzerova et al. 2009, 2010, 2012). This shift in sympathovagal cardiac control, along with electrodermal hypoactivity, could reflect a specific effect on different effector systems of autonomic imbalance in MDD patients.

5 Conclusions

The present study revealed altered sympathetic cholinergic regulation, expressed by electrodermal hypoactivity, in untreated major depression in adolescence. This finding underscores the significance of potential autonomic-mediated risk of early negative health outcomes in depressed patients in a vulnerable adolescent age-period. The exact autonomic regulatory mechanisms underlying the central-peripheral interaction in depressive disorder remain to be further explored by alternative study design.

Acknowledgments This work was supported by National Research Grant VEGA 1/0087/14, Comenius University Grant UK/151/2016, and the project "Biomedical Center Martin" ITMS code: 26220220187, the project is co-financed from EU sources.

Conflicts of Interest The authors declare no conflicts of interest in relation to this article.

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