Neuroscience Letters 640 (2017) 6–12

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Research article

Antidepressant and anxiolytic-like behavioral effects of erucamide, a bioactive fatty acid amide, involving the hypothalamus–pituitary–adrenal axis in mice

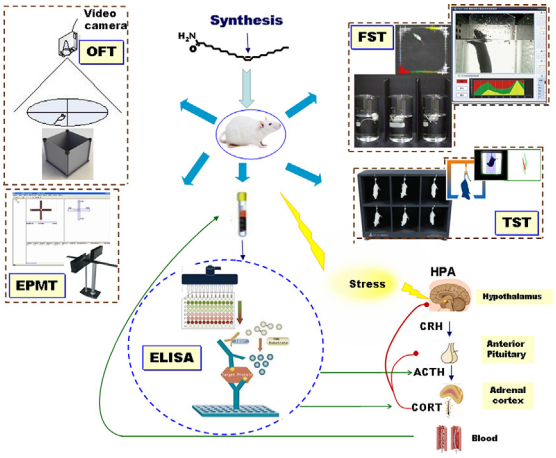
Miao-Miao Li[a,1], Zheng-er Jiang[b,1], Ling-Yun Song[a], Zhe-Shan Quan[c,*], Hai-Ling Yu[a,*]

[a] College of Medicine, Yanbian University, Park street 977, Yanji, 133002, Jilin, PR China
[b] College of Nursing, Yanbian University, Park street 977, Yanji, 133002, Jilin, PR China
[c] College of Pharmacy, Yanbian University, Park street 977, Yanji, 133002, Jilin, PR China

HIGHLIGHTS

- TST and FST induced depression-like behaviors in mice.
- EPMT and OFT induced anxiety-like behaviors in mice.
- Erucamide, a bioactive fatty acid amide, ameliorated mouse depression and anxiety like behaviors.
- ACTH and CORT serum levels in Erucamide treatment mice were reduced compared to the control group.
- Erucamide may be involved in hypothalamus–pituitary–adrenal axis regulation.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 7 November 2016
Received in revised form
16 December 2016
Accepted 30 December 2016
Available online 10 January 2017

Keywords:
Erucamide
Depression
Anxiety disorder
HPA axis
Mice

ABSTRACT

Erucamide (Era) is a bioactive fatty acid amide, which is similar to the classical endocannabinoid analogue oleoylethanolamide (OEA). In the present study, we hypothesized that Era may regulate the central nervous system and may have the potential to antagonize depression and anxiety. Therefore, we investigated the antidepressant and anxiolytic effects of Era in animal models in comparison with fluoxetine (Fxt). Fifty mice were randomly divided into 5 groups, and treated with a vehicle (0.3% methyl cellulose, 20 mL/kg, p.o.), Era (5, 10, 20 mg/kg, p.o.), or Fxt (20 mg/kg, p.o.) for 7 days. Immobility was used to evaluate depressive-like behavior in the forced swimming test (FST) and tail suspension test (TST). Animal activity and exploratory behavior as well as anxiety-like behaviors were measured in open field test (OFT) and elevated plus-maze test (EPMT) in mice. Additionally, serum adrenocorticotrophic hormone (ACTH) and corticosterone (CORT) levels were determined using the ELISA method, and the total anti-oxidative capacity (T-AOC) was detected by ultraviolet spectrophotometry. Our data showed that Era (5, 10, or 20 mg/kg) induced a significant reduction in mouse immobility time in the TST and FST compared to the normal control group (vehicle group). The positive control, Fxt (20 mg/kg group), also induced a significant change in immobility time in the TST and FST compared to the control (vehicle)

* Corresponding authors.
E-mail addresses: zsquan@ybu.edu.cn (Z.-S. Quan), hlyu@ybu.edu.cn (H.-L. Yu).
[1] First authors.

http://dx.doi.org/10.1016/j.neulet.2016.12.072
0304-3940/© 2017 Elsevier B.V. All rights reserved.

group. In the OFT, compared with the control group, Fxt (20 mg/kg) and Era (5, 10, or 20 mg/kg) did not significantly change the locomotive activity (locomotive time, immobility time, or locomotive distance) in mice, but Fxt (20 mg/kg) and Era (10, or 20 mg/kg) significantly increased the percentage of time spent and squares visited in the OFT central area. In regards to the EPMT, the data showed that Fxt (20 mg/kg) and Era (10, 20 mg/kg) significantly increased the ratio of time spent and entries in open arms, but did not significantly change the total locomotive distance (including open arms and closed arms) compared to the control group. Biochemical tests found that after 7 days of drug treatment, compared with the control group, ACTH and CORT serum levels in mice were significantly decreased, although T-AOC levels did not significantly change. In conclusion, Era (dose range of 5–20 mg/kg) administered orally may alleviate depression- and anxiety-like behaviors in mice, and the antidepressant and anti-anxiety effects of Era may be related to the regulation of the hypothalamus–pituitary–adrenal axis (HPA).
© 2017 Elsevier B.V. All rights reserved.

1. Introduction

Depression is a severe psychiatric disorder with a lifetime prevalence in excess of 15%. Depression and anxiety disorders have increasingly plagued people in modern life [1]. The hypothalamic–pituitary–adrenal (HPA) axis is a major integrated system that maintains body homeostasis, which controls the stress responses of an individual [2]. Its dysfunction may be important in the pathogenesis of depression [3], and the HPA axis is an emerging target in the treatment of depression. In recent years, numerous studies have also demonstrated that the HPA axis may be important for the clinical efficacy of antidepressant treatment [4].

Erucamide ((*Z*)-docos-13-enoic acid), with a molecular formula of $C_{22}H_{42}O_2$ and a structural formula shown in Fig. 1, was found to be the major bovine mesentery angiogenic lipid as assessed by the chorioallantoic membrane (CAM) assay [5]. In Wakamatsu's assay, 2 mg of this lipid caused angiogenesis and angiogenic activity. This naturally occurring lipid was also found by rat corneal micropocket and mouse dorsal air-sac assays. However, the specificity of the chemical structure that elicited the activity was low [5].

There are a large number of saturated or unsaturated fatty acid amides in living organisms. Their high biological activity, receptor-mediated mechanisms of action, and specific biosynthesis and degradation pathways suggest that they may be a new class of biological regulatory molecules. Fatty acid amides participate in the adjustment of many biological functions as the endogenous bioactive lipid. In addition, fatty acid amides are also associated with many other lipid-regulating molecules. This family consists of fatty acid ethanolamide (such as anandamide, palmitoyl ethanolamine and oleoylethanolamide) and fatty acid primary amides (such as oleamide and erucamide). Previous studies have shown that endogenous fatty acid amides have significant central and peripheral bioactivity [6–9]. Yang et al. (1998) found the sedative and hypnotic effects of oleamide (OLA) in mice. Additionally, increasing evidence suggests that oleoylethanolamide (OEA) and palmitoyl ethanolamine (PEA) may act as endogenous neuroprotective factors and participate in the control of reward-related behaviors. Yu et al. [8,9] indicated that boosting OEA and PEA tone may be a useful alternative therapeutic approach for depressive disorders. In recent years, their biological significance and mechanisms are being extensively studied, and a positive exploration in the field is also a topic of interest by our research group.

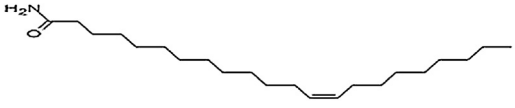


Fig. 1. The structure of erucamide.

Our previous studies have confirmed that OEA and PEA have antidepressant activity. However, in terms of bioactivity of erucamide, there are few reports in the literature. Furthermore, as it is unclear whether orally administered erucamide (Era) is effective against depression and anxiety, the regulation of circulating Era during stress needs to be addressed in further studies. In the present study, the antidepressant and anxiolytic effects of Era were tested in comparison with the antidepressant fluoxetine (Fxt) using the mouse forced stress models. Additionally, in neurochemical studies, changes in serum adrenocorticotropic hormone (ACTH) and corticosterone (CORT) levels were measured to investigate whether the mechanism of action is related to the regulation of HPA-axis activity.

2. Materials and methods

2.1. Approval

All experimental procedures were approved by the Institutional Animal Care Committee of Yanbian University.

2.2. Materials

The mouse CORT and ACTH ELISA kit were purchased from Shanghai Enzyme linked Biotechnology Co., Ltd., China. The T-AOC kit was purchased from Nanjing Jiancheng Bioengineering Institute, China. The tested compounds erucamide (purchased from Jkchemical Co., Ltd., Beijing, China) or fluoxetine (Fxt, Enhua Jiangsu Pharmaceutical Co., Ltd., China) were resuspended in 0.3% methyl cellulose (Loba-Chemie, Shanghai, China) and administered daily via gavage. All of the doses were expressed as milligrams per kilogram body weight of the respective drugs.

2.3. Animals

Male adult Kunming mice (A closed colony mice, derived from Swiss mice) weighing 18–22 g were purchased from Laboratory Animal Center of Yanbian University. The mice were housed in cages for 3 days to adapt to the environment under controlled conditions of 12 h light–12 h dark cycles, and had free access to food pellets and tap water. The ambient temperature and relative humidity were maintained at 22 ± 2 °C and 55% ± 5%, respectively. Animals are subjected to a certain mild acclimation process before the test. All animal experiments were approved by the Animal Care and Use Committee of the China Pharmaceutical University and complied with the Declaration of the National Institutes of Health Guide for Care and Use of Laboratory Animals (Publication No. 85-23, revised 1985).

Download English Version:

https://daneshyari.com/en/article/5738811

Download Persian Version:

https://daneshyari.com/article/5738811

Daneshyari.com