إمكانية تحسن الإكتئاب الناشئ من إستئصال المبيض في الجرذان بواسطة الديهيدروايبى اندروستيرون و الإشنسيا و السرترالين

رسالة مقدمة
للحصول على درجة دكتوراه الفلسفة في العلوم
(علم الحيوان)
من

هــند أحـمـد صبري

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2010

Ain Shams University
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POSSIBLE AMELIORATION OF OVARIECTOMY INDUCED DEPRESSION IN RATS WITH DHEA, ECHINACEA AND SERTRALINE

THESIS
Submitted for the Degree of Philosophy Doctor (Ph. D.) in Zoology

By

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ACKNOWLEDGMENT

First of all, thank **God** for giving me the effort to finish this work.

No words can be good enough to express my deepest gratitude and sincere appreciation to **Prof. Dr. Ahmed Refaat Ezzat**, Professor of Physiology, Zoology Dept., Faculty of Science, Ain Shams University, for suggesting the problem, supervising the whole work and the critical reading of the manuscript.

I'm greatly indebted to **Prof. Dr. Afaf A. Abo-Nour** Professor of Physiology, University College for Women, Arts, Science and Education, Ain Shams University, for sharing in planning and supervision this work. I also appreciate her kind encouragement, valuable advice and her contribution in reading the manuscript.

I'm also greatly indebted to **Dr. Nadia Mohamed Saaid Arafa,** Associate Professor of Physiology, the National Organization for Drug Control and Research (NODCAR) for devoting her efforts throughout all the stage of development of this work, for her kind encouragement and for providing the laboratory facilities needed to complete this work.

I would like also to express my deepest thanks to **Dr. Elham Ali Hassan**, Lecturer of Zoology, University College for Women, Arts, Science and Education, Ain Shams University, for sharing and helping in the experimental work and supervision of this investigation.

I would like to acknowledge the cooperation and support of all my colleagues and members of the Zoology Department. Finally, with all the gratitude and love i shall always remember the kind care and the support of my family.

ABSTRACT

POSSIBLE AMELIORATION OF OVARIECTOMY INDUCED DEPRESSION IN RATS WITH DHEA, ECHINACEA AND SERTRALINE

Depression is one of the most widespread diseases that affect all ages and women more than men, most antidepressant medication on the market today can cause serious side effects, and many of them may come now with a "Black Box Warning." This study was planned to evaluate the ameliorative potentials of the neuro-active natural steroid hormone dehydroepiandrosterone (DHEA), the specific serotonin reuptake inhibitor antidepressant drug sertraline (S) and the natural herb Echinacea (Ech) on depression in female rats experimentally induced by ovariectomy.

Adult four months old female rats (130-150 gm) were divided into 2 mains groups: one was maintained as a normal intact group. The rats of the second group were further subdivided into 2 groups. The first was sham operated and the other was ovariectomized. The forced swimming test (FST) was then applied to the ovariectomized rats to eliminate those which did not exhibit depressed behavior. The rats that tested positive in the FST were classified as ovariectomized depressed (OVX-d) rats. The normal intact group and OVX-d rats were divided into four subgroups; the first was left without further treatment and referred to as the control group, and the other three subgroups were treated with one of the following drugs: DHEA (25 mg/kg/day), sertraline (50mg/kg/day) and Echinacea (60 mg/kg/day). After 3 weeks, half of the rats in each group were removed for autopsy and the rest were treated for further 3 weeks before performing autopsy. After decapitation, the brain was immediately excised and dissected into the hypothalamus, cerebellum, mid brain, frontal cortex and pons. The monoamine neurotransmitters norepinephrine (NE), serotonin (5-HT) and dopamine (DA) in addition to the peptide

neurotransmitters GABA, β-endorphine and methonine-enkephaline (M-enkephaline) were determined. Blood was collected to determine the serum hormones (DHEA, testosterone, 17β-estradiol, corticosterone, prolactin (PRL)), serum interleukine-2 (IL2) and the lymphocyte viability.

The present results revealed that the treatment with DHEA, S and Ech caused a significant increase in the NE, DA, 5-HT, GABA, and β-endorphine in all investigated brain areas in comparison with the control group. Also, these treatments induced an increase in serum hormones DHEA, testosterone, 17β-estradiol, whereas a decrease in corticosterone and prolactin (PRL) were recorded. Moreover, an increase in (IL-2) and the lymphocyte viability was noticed in comparison with the normal and sham operated group.

Ovariectomy caused a general decrease in the studied neurotransmitters in comparison with the normal and sham operated groups. Also, ovariectomy induced a decrease in serum DHEA, testosterone, 17β-estradiol, whereas an increase in corticosterone and prolactin (PRL) was recorded. A decrease in (IL-2) and the lymphocyte viability was noticed in comparison with the normal and sham operated group.

Treatment of the OVX-d with DHEA, S and Ech induced a significant improvement in the FST in comparison with the depressed rats after 6 weeks. These treatments caused a significant increase in NE, 5-HT, DA, GABA, and β-endorphine in all investigated brain areas in comparison with those of the OVX-d rats. In addition, these treatments restored the levels of these neurotransmitters in OVX-d rats to values close to the range of the normal and sham operated after 6 weeks. Treatment with DHEA or Ech caused a significant increase in frontal cortex M-enkephaline content as compared with the OVX-d rats. Pons M-enkephaline content was significantly elevated by DHEA, S or

Ech at 6 weeks of treatment. The results indicated that the treatment with DHEA, S or Ech caused an improvement in serum hormone levels as compared with control and sham operated after 6 weeks of treatment. Serum IL-2 content and lymphocyte viability showed a significant increase in DHEA and Ech treated rats, whereas a significant decrease in S treated group in comparison with the normal and sham operated after 6 weeks of treatment.

It is concluded that treatment of rats with DHEA, S or Ech caused a partial protection against depression induced by ovariectomy. This was indicated by increasing the neurotransmitters, serum hormones (DHEA, testosterone and 17β-estradiol), lymphocyte viability, IL2 and reducing corticosterone and prolactin (PRL). The results also indicated that DHEA is more effective in treatment the depression than S and Ech. The present study demonstrates that S and Ech possess a protective effect on the brain against OVX-d rats. Echinacea treatment caused an improvement, not only in immune functions, but also in the monoamines, GABA and opioid levels. These results may provide additional information about ovariectomy induced depression and possible manipulations of its consequences using three different approaches; hormonal (DHEA), pharmaceutical (sertraline) and herbal (Echinacea).

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عنوان الرســالة: إمكانية تحسن الإكتئاب الناشئ من إستئصال المبيض في الجرذان بواسطة الديهيدروايبى اندروستيرون و الإشنسيا والسرترالين

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الدراسات العليا

ختم الإجازة
/ /2010

اجيزت الرسالة

موافقة مجلس الكلية
/ / 2010

موافقة مجلس الجامعة
/ /2010

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سنـة المنـــــح: ã2010