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ORIGINAL ARTICLE

Temporary amygdala inhibition reduces stress effects in female mice

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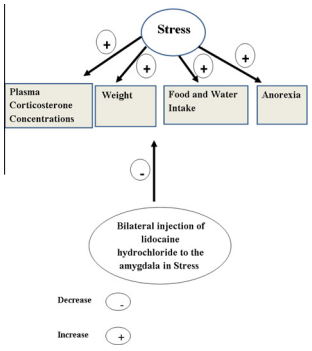
GRAPHICAL ABSTRACT



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ABSTRACT

The current study investigated the effect of temporary inhibition of amygdala in response to metabolic changes caused by stress in female mice. Unilateral and bilateral amygdala cannulation was carried out, and after a week of recovery, 2% lidocaine hydrochloride was injected into the mice amygdalae five minutes before the induction of stress. A communication box was employed to induce stress for four consecutive days and plasma corticosterone, food and water intake, weight changes, and anorexia were measured as stress-induced metabolic changes. Results demonstrated that stress, increases stress, increased plasma corticosterone concentrations, weight, food, and water intake. Temporary inhibition of the amygdala slightly decreased plasma corticosterone concentrations, but did not fully reduce the effect of stress. The bilateral injection of lidocaine hydrochloride to the amygdala reduced the effect of stress and reduced water intake and weight. Unilateral injection of lidocaine hydrochloride into the left and right amygdala reduced food intake. In conclusion, the present study demonstrated that the left side and right side of amygdala nuclei play a different role in metabolic responses in stress.

Introduction

Stress is an inevitable part of the modern world, and a factor in the expression of disease. Maintaining stability of the body's internal environment (homeostasis) in the presence of stressors needs several complex responses, such as the endocrine, the nervous, and the immune system activities known as the stress response. In other words, several behavioral and physiological changes were initiated in response to stress in order to increase survival when stability of homeostasis is threatened. Poor regulation of the internal environment in response to stress leads to pathological responses such as high blood pressure, mood disorders, and depression [1,2]. Although the central nervous system is involved in maintaining stability of homeostasis and organization of stress responses, certain cerebral areas also play a major role in this regulatory mechanism, such that mood disorders may result to a dysfunctional limbic system or hypothalamus–pituitary–adrenal (HPA) axis [3–7].

Amygdala, the major part of the limbic system, plays a central role in processing emotional states and organizing the response to stress [8]. Stimulation of the amygdala neurons produces corticotropin-releasing factor (CRF) and releases them into the blood. The amygdala is known as the center of cardiovascular and behavioral response to stress and also engages in emotional responses, especially in the case of fear and dread. These responses result in the release of stress hormones and changes in blood pressure and heart rate [9,10]. Amygdala reduces stress-induced changes in swallowing behavior and has a more prominent role in psychological stress. Moreover, there are structural differences between the left and right amygdalae, and the stimulation of the right amygdala induces negative emotions, especially fear, while the stimulation of the left amygdala induces good (happiness) and bad (stress) feelings simultaneously [8].

Gender differences in the incidence and prevalence of psychological disorders related to stress have been offered; for instance, when women and men experience the same stressors, women may be more prone than men to develop depression [11]. Previous studies have demonstrated that amygdala is one of the best known cerebral areas associated with gender differences. It is known that the amygdala is larger in adult males than in females [12,13]. Furthermore, amygdala has a central role in remembering emotional experiences, and it has been shown that, on average, women have a stronger memory for recollecting emotional events when compared to men [14]. Thus, there is a difference between the male and female amygdala and left amygdalae and right amygdalae have different roles in the responses to stress. Therefore, examining this bias in the response to stress is important. Hence, the present study was carried out to investigate the effect of the temporary inhibition of the left and right amygdala in response to the hormonal and metabolic changes caused by stress in female mice.

Material and methods

Animals

Female NMRI mice weighing 25 ± 5 g were kept in groups of six per cage in 12/12 light/dark conditions at 22–24 °C, with food and water provided *ad libitum*. The animals were randomly divided into control and experimental groups (n = 6/group). The food and water intake was recorded for each animal at specific hours every day. Vaginal smears were taken from all the animals in the control and stress group in order to determine their phase of sexual maturity before commencing the tests; the tests started in the proestrus phase. *Animal experiments were conducted in accordance with the Guidelines of the National Institute of Health (NIH) for the Care and Use of Laboratory Animals, and were approved by the local ethical committee (The Baqiyatallah University of Medical Sciences Committee on the Use and Care of Animals, 87/381).*

Animal group

Animals were randomly divided into eight groups (n = 6). Group 1 (control) received no treatment and group 2 (stress) received 4 days stress. Three groups of animals were injected