Bull Yamaguchi Med Sch 46(3-4) : 81-82, 2000

Mechanisms of induction of stress-induced endocrine, febrile and cardiovascular responses

Tatsuo Watanabe

Department of Physiology, Tottori University Faculty of Medicine, Yonago, Tottori 683, Japan.
(Received September 14, 1999, revised September 29, 1999)

Key Words: Interleukin-1, Exercise, ACTH, Fever, Blood pressure

Introduction

Animals exposed to stressors usually show activation of the sympathetic nervous system and the hypothalamo-pituitary adrenocortical axis, with consequent increases in body temperature, blood pressure, heart rate and the plasma concentration of adrenocorticotropic hormone (ACTH). This review focuses on the mechanism of induction of the stress-induced responses.

Role of prostaglandin E (PGE) in the stress-induced ACTH response

It is widey accepted that PGE acts as a final mediator to induce febrile responses when immunological stressors [such as interleukin-1 (IL-1)] are given to animals[1]. We hypothesized that PGE is responsible for the induction of the immunological stress-induced ACTH response. Our results showed an increase in plasma concentration of ACTH after systemic injection of IL-1, and its inhibition by PG synthesis inhibitor, indomethacin, indicating that PGE is involved in the IL-1-induced ACTH reponse[2-5]. Furthermore, we demonstrated that PGE plays an important role in non-immunological stress-induced ACTH responses. For example, injection of indomethacin led to an inhibition of an increase in plasma level of ACTH induced by cage-switch stress[6] or swimming exercise[7]. Finally, intrahypothalamic administration of PGE produced ACTH response that was completely suppressed by injection of anti-corticotropin-releasing factor (CRF) antibody[4]. Taken together, it is likely that immunological and non-immunological stresses stimulate synthesis and release of PGE within the hypothalamus, which induces ACTH response through the mediation of the hypothalamic hormore, CRF.

Role of angiotensin II (ANG II) and its receptors within the brain in the stress-induced cardiovascular and febrile responses

ANG II has recently been recognized as one of the stress-related hormones that participate in various stress-induced responses[8]. We have shown that ANG II receptors within the brain contribute to the induction of the stress-induced responses.

Rats exposed to restraint stress (non-immunological stress) had increases in blood pressure, heart rate and body temperature that were significantly reduced by treatment with intracerebroventricular (i.c.v.) injection of ANG II type 1 receptor (AT_1-receptor) antagonist, losartan[9]. The activation by restraint stress of the sympathetic nervous system was inhibited by i.c.v. losartan as shown by the suppression of the stress-induced increases in plasma concentration of norepinephrine and epinephrine[9]. These results suggest that brain AT_1-receptors are involved in the induction of the non-immunological stress-induced responses.

The systemic injection of IL-1 or i.c.v.

injection of PGE (immunolgical stress) resulted in increases in body temperature. These febrile responses were attenuated by i. c.v. injection of ANG II type 2 receptor (AT_2-receptor) antagonist, CGP 42112A, while AT_1-receptor antagonist had no effect[10]. It is likely that immunological stress elicits increases in body temperature through the mediation or modulation by the brain AT_2-receptors.

Concluding remarks

In this review, I summarized the role of PGE and ANG II receptors in the induction of stress-induced endocrine, febrile and cardiovascular responses. PGE, which is synthesized and released in response to immunological or non-immunological stress, acts within the hypothalamus to stimulate the secretion of CRF into the hypophyseal portal vein, leading to the ACTH response. On the other hand, brain AT_1-receptors contribute to the induction of non-immunological stress-induced cardiovascular and hyperthermic responses, while febrile response induced by immunological-stress is at least in part attributable to the mediation or modulation by the brain AT_2-receptors. In future research, cellular or molecular mechanism of induction of stress responses should be extensively investigated.

References

1) Kluger,M.J. : Fever : Role of pyrogens and cryogens. *Physiol.Rev.*, **71** : 93-125, 1991.

2) Morimoto, A., Murakami, N., Nakamori, T., Sakata,Y.and Watanabe,T.:Possible involvement of prostaglandin E indevelopment of ACTH response in rats induced by human recombinant interleukin-1. *J. Physiol. (Lond.)*, **411** : 245-256, 1989

3) Murakami,N. and Watanabe,T : Activation of ACTH release is mediated by the same molecule as the final mediator, PGE_2, of febrile response in rats. *Brain Res.*, **478** : 171-174, 1989.

4) Watanabe, T., Morimoto, A., Sakata, Y. and Murakami, N. : ACTH response induced by interleukin-1 is mediated by CRF secretion stimulated by hypothalamic PGE. *Experientia*, **46** : 481-484, 1990.

5) Watanabe, T., Morimoto, A. and Murakami,N. : ACTH respnose in rats during biphasic fever induced by interleukin-1. *Am.J.Physiol.*, **261** : R1104-R1108, 1991.

6) Morimoto, A., Watanabe, T., Morimoto, K., Nakamori, T. and Murakami, N. : Possible involvement of prostglandins in psychological stress-induced respnses in rats. *J.Physiol. (Lond)*, **443** : 421-429, 1991.

7) Watanabe, T., Morimoto, A., Sakata, Y., Long, N.C. and Murakami, N. : Prostaglandin E_2 is involved in adrenocorticotrophic hormone release during swimming exercise in rats. *J.Physiol. (Lond..)*, **433** : 719-725, 1991,

8) Watanabe, T., Fujioka, T., Hashimoto, M. and Nakamara, S.: Stress and brain angiotensin II receptoqrs. *Crit. Rev. Neurobiol.*, **12** (4) : 305-317, 1998.

9) Saiki, Y., Watanabe, T., Tan, N., Matsuzaki, M. and Nakamura, S. : Role of central ANG II-receptors in stress-induced cardiovascular and hyperthermic responses in rats. *Am.J.Physiol.*, **272** : R 26-R33, 1997.

10) Watanabe, T., Saiki, Y and Sakata, Y. : The effect of central angiotensin II receptor blockade on interleukin-1β-and prostaglandin E-induced fevers in rats:possible involvement of brain angiotensin II receptor in fever induction. *J.Pharmacol. Exp.Ther.*, **282** : 873-881, 1997.