A MINI-REVIEW ON THE ROLE OF ANGIOTENSIN II AND ITS RECEPTORS IN THE DEVELOPMENT OF FEVER IN RODENTS

T. Watanabe, Department of Physiology, Tottori University, Yonago, Japan.

Angiotensin II (ANG II) has recently been recognized as one of the stress hormones that participate in various stress-induced responses, including hyperthermic response. Fever may be one of the stresses (i.e., immunological stress), because the stimuli that induce fever stimulate the hypothalamo-pituitary-adrenocortical axis and sympathetic nervous system. Recent studies have revealed the existence of two types of ANG II receptors in the brain, AT_1 and AT_2. In this mini-review, we summarizes our findings on the role of ANG II and its receptors in the development of fever in rodents. We report an inhibition by intrahypothalamic (i.h.) injection of AT_2 receptor antagonist (5 μg) of the fever induced in rats by intraperitoneal (i.p.) injection of interleukin-1 (IL-1, 2 μg/kg) or i.h. prostaglandin E (PGE, 100 ng). The PGE-induced fever in rats was enhanced by treatment with ANG II (25 ng, i.h.) but was reduced by angiotensin converting enzyme (ACE) inhibitor (10 μg, i.h.). ANG II alone had no effect on the resting body temperature. Moreover, we present our results showing an attenuation of IL-1 (10 μg/kg, i.p.)-induced fever in the AT_2 receptor-deficient mice. It is, therefore, likely that AT_2-receptors contribute to the fever induction in mice as well as in rats, and that hypothalamic AT_2-receptors modulate the PGE fever in a positive way at the final step of fever induction. On the other hands, we present in this mini-review our very recent results showing that the fever induced in dehydrated rats by intravenous (i.v.) injection of lipopolysaccharide (LPS, 2 μg/kg) was attenuated by systemic administration of ACE inhibitor (10 mg/kg, i.v.), while the fever induced by IL-1 (2 μg/kg, i.v.) was not. These results suggest that ANG II is involved in the development of fever induced in dehydrated rats by i.v. injection of LPS via stimulating the production of pyrogenic cytokines, such as IL-1. Taken together, it is likely that ANG II and AT_2 receptors contribute to the induction of fever at the final step by affecting the processes mediated by PGE, and that ANG II participates, at the first step of fever induction, in the synthesis and release of pyrogenic cytokines in response to LPS.

watanabe@grape.med.tottori-u.ac.jp