学位論文抄録

Chronic Angiotensin 1-7 Infusion Prevents Angiotensin-II-Induced Cognitive Dysfunction and Skeletal Muscle Injury in a Mouse Model of Alzheimer's Disease

（アンギオテンシン 1-7 の慢性投与はアルツハイマー病モデルマウスのアンギオテンシン II による認知機能障害と骨格筋傷害を抑制する）

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Abstract of the Thesis

Background and Purpose: Alzheimer's disease (AD) is increasingly viewed as a neurological disease accompanied by a systemic disorder. Accumulating evidence supports that angiotensin II and angiotensin 1-7 exert opposite effects on various organs including the brain. However, the interaction between angiotensin II and angiotensin 1-7 in AD remains to be defined. The present study was undertaken to examine the interaction between these peptides in AD.

Methods: 5XFAD mice, a useful model of AD, were separated into three groups: 1) saline-infused, 2) angiotensin II-infused, and 3) angiotensin II-infused and angiotensin 1-7-co-infused. These peptides were systemically given to 5XFAD mice via osmotic minipump for 4 weeks.

Results: Systemic angiotensin II infusion for 4 weeks induced significant hypertension in both wild-type and 5XFAD mice. Angiotensin II induced cognitive abnormality in 5XFAD mice as estimated by the Morris water maze test and the nest building test, and this effect was associated with cerebral blood flow reduction, cortical arterial amyloid β deposition, hippocampal inflammation, and neuron loss in 5XFAD mice. In addition, angiotensin II infusion led to gastrocnemius muscle atrophy in 5XFAD mice. Co-infusion of angiotensin 1-7 prevented the above mentioned detrimental effects of angiotensin II in the brain and gastrocnemius muscle in 5XFAD mice, without significant influence on blood pressure. The left ventricular hypertrophic response to angiotensin II was attenuated in 5XFAD mice compared with wild-type mice, which was not significantly altered by co-administration of angiotensin 1-7.

Conclusions: Our results show that angiotensin 1-7 counteracts angiotensin II-induced cognitive impairment, brain injury, and skeletal muscle injury in AD mice.