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PROTECTIVE ROLE OF ANGIOTENSIN(1-7) AGAINST ANGIOTENSIN II-INDUCED COGNITIVE DYSFUNCTION IN ALZHEIMER'S DISEASE MOUSE

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Purpose: Renin-angiotensin system (RAS) is supposed to participate in the pathophysiology of cognitive impairment and Alzheimer's disease (AD). Emerging evidence suggests the new concept that angiotensin (1-7)/MAS system exists independently of classical RAS system and can potentially counteract classical RAS system. The present study was performed to examine whether angiotensin (1-7) can protect against angiotensin II-induced cognitive impairment in AD mouse. **Methods:** 5XFAD mice, a useful model of AD, were separated into 3 groups: (1) saline-infused group (control), (2) angiotensin II-infused group, and (3) angiotensin II-infused and angiotensin (1-7)-infused group. Each peptide was subcutaneously infused to 5XFAD mice via osmotic minipump for 4 weeks, and cognitive function and brain injury were compared among the 3 groups. **Results:** All significantly increased blood pressure in 5XFAD mice and angiotensin (1-7) did not modify All-induced hypertension. As estimated by Morris Water maze test and nest building test, All significantly impaired cognitive function in 5XFAD mice. However, angiotensin (1-7) ameliorated All-induced cognitive dysfunction. Cerebral blood flow in 5XFAD mice was significantly decreased by All, and this decrease was attenuated by angiotensin (1-7) coadministration. Amyloid β deposition in cerebral cortical artery of 5XFAD mice was increased by All infusion, and this increased amyloid β deposition was significantly ameliorated by angiotensin (1-7). **Conclusion:** Taken together with our previous reports (Exp Gerontol (2017); JAHA (2017)), our results suggest that angiotensin (1-7) can counteract angiotensin II-induced brain injury in AD independently of blood pressure, thereby highlighting angiotensin (1-7) as a potential therapeutic agent for AD.



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