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Br J Pharmacol. 2015 Aug;172(15):3764-78. doi: 10.1111/bph.13172. Epub 2015 Jun 12.

## Lack of weight gain after angiotensin AT1 receptor blockade in diet-induced obesity is partly mediated by an angiotensin-(1-7)/Mas-dependent pathway.

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### Abstract

**BACKGROUND AND PURPOSE:** Angiotensin AT1 receptor antagonists induce weight loss; however, the mechanism underlying this phenomenon is unknown. The Mas receptor agonist angiotensin-(1-7) is a metabolite of angiotensin I and of angiotensin II. As an agonist of Mas receptors, angiotensin-(1-7) has beneficial cardiovascular and metabolic effects.

**EXPERIMENTAL APPROACH:** We investigated the anti-obesity effects of transgenically overexpressed angiotensin-(1-7) in rats. We secondly examined whether weight loss due to telmisartan (8 mg·kg<sup>-1</sup>·d<sup>-1</sup>) in diet-induced obese Sprague Dawley (SD) rats can be blocked when the animals were co-treated with the Mas receptor antagonist A779 (24 or 72 µg·kg<sup>-1</sup>·d<sup>-1</sup>).

**KEY RESULTS:** In contrast to wild-type controls, transgenic rats overexpressing angiotensin-(1-7) had 1.) diminished body weight when they were regularly fed with chow; 2.) were protected from developing obesity although they were fed with cafeteria diet (CD); 3.) showed a reduced energy intake that was mainly related to a lower CD intake; 5.) remained responsive to leptin despite chronic CD feeding; 6.) had a higher, strain-dependent energy expenditure, and 7.) were protected from developing insulin resistance despite CD feeding. Telmisartan-induced weight loss in SD rats was partially antagonized after a high, but not a low dose of A779.

**CONCLUSIONS AND IMPLICATIONS:** Angiotensin-(1-7) regulated food intake and body weight and contributed to the weight loss after AT1 receptor blockade. Angiotensin-(1-7)-like agonists may be drug candidates for treating obesity.

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PMID: [25906670](#) PMIDID: [PMC4523334](#) [Available on 2016-08-01] DOI: [10.1111/bph.13172](#)

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