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Effect of non-classical renin-angiotensin system stimulation in metabolically active tissues of obese Zucker rats

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Local renin-angiotensin system (RAS) in the skeletal muscle and adipose tissue is of physiological relevance. Angiotensin 1-7 (Ang 1-7) enhances insulin signalling and glucose transport activity in both tissues. The major limitation of exogenous administration of Ang 1-7 is that it is a peptide with short biological half-life. AVE0991, a non-peptide Mas-receptor agonist, has been reported to mimic the action of Ang 1-7. Furthermore, diminazene aceturate (DIZE) was identified as an activator of angiotensin-converting enzyme 2. The aim of our study was to evaluate the effect of AVE0991 and DIZE application on metabolic parameters, expression of the RAS components and markers of oxidative stress, and activity of aminopeptidase A (APA) in the skeletal muscle and adipose tissue of obese Zucker rats.

Administration of DIZE lowered APA activity in adipose tissue, which might have a beneficial role, since APA degrades Ang 1-7. AVE0991 treatment improved whole body glucose utilization, downregulated the expression of angiotensin-converting enzyme (ACE) and NADPH oxidase 4 (NOX4) in adipose tissue, and enhanced the expression of renin receptor, transcription factor PLZF, NOX4 and superoxide dismutases 1 and 2 in skeletal muscle. It has been shown that reactive oxygen species (ROS) have insulin-mimetic action in muscle. The improved glucose tolerance after AVE0991 treatment might occur due to enhanced ROS production in the skeletal muscle. However, excessive production of ROS in adipose tissue due to ACE/Ang II/AT1 axis might impair insulin signalization. The decline in ACE and NOX4 expression in epididymal fat after AVE0991 administration might have a beneficial role on adipocyte glucose uptake.

Our results suggest that AVE0991 treatment triggers different mechanisms in skeletal muscle and adipose tissue improving the insulin signalling cascade, which needs further investigation.

Biography

Viktória Lory is currently doing her PhD at the Institute of Experimental Endocrinology, Biomedical Centre, Slovak Academy of Sciences.

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