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17Beta-estradiol Stimulates Glucose Uptake Through Estrogen Receptor and AMP-activated Protein Kinase Activation in C2C12 Myotubes (Korean J Obes 2016;25:190-6)

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Long-term 17beta-estradiol treatment protects against obesity, glucose intolerance and insulin resistance in obese and insulin-resistant ovariectomized rodents[1-3], and long-term hormone therapy prevents diabetes mellitus due to alterations in body fat distribution and insulin sensitivity, but short-term hormone therapy does not provide complete protection in postmenopausal women.[4,5]

17beta-estradiol acts predominantly through genomic pathways and regulates the expression of a number of genes by binding to estrogen receptor α and β.[6] However, the activation of non-genomic or rapid signaling pathways in response to 17beta-estradiol has attracted increasing attention.[7,8] Acute treatment (≤ 10 minutes) with 17beta-estradiol rapidly increases the phosphorylation of Akt and AMPK, possibly through non-genomic effects, while it does not stimulate glucose uptake or enhance insulin sensitivity in skeletal muscles (rat soleus) *ex vivo*.[9] We investigated whether 24-hour treatment with 17beta-estradiol stimulates glucose uptake and regulates the expression of genes associated with glucose metabolism through the genomic effects of estrogen receptor in C2C12 myotubes. In this study, 24-hour treatment with 17beta-estradiol stimulated glucose uptake, but 30-minute treatment did not. We could not determine the potential mechanisms through which 17beta-estradiol stimulated the expression of genes associated with glucose uptake in C2C12 myotubes, which was a limitation of the study. Further investigation of possible mechanisms will be needed.

As a reader mentioned, mitochondria may be associated with a potential mechanism by which 17beta-estradiol treatment stimulates glucose uptake in C2C12 myotubes, and AMPK stimulates mitochondrial biogenesis by regulating PGC-1α, which in turn promotes transcription of genes in mitochondria and the anti-oxidant defense system.[10] We could not investigate these mechanisms. We postulate that 17beta-estradiol regulates the expression of genes associated with glucose metabolism through the genomic effects of estrogen receptor in promoters of genes associated with glucose metabolism.

As a reader suggested, the role of estrogen in mitochondria, which is associated with glucose uptake in skeletal muscle, remains to be investigated, and measurement of the effects of estrogen on fatty acid oxidation in skeletal muscle would also be useful. We agree that

these avenues of future research could provide insight into the mechanism of action of 17beta-estradiol in glucose metabolism.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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