Lack of skeletal muscle IL-6 influences hepatic glucose metabolism in mice during prolonged exercise

The liver is essential in maintaining and regulating glucose homeostasis during prolonged exercise. IL-6 has been shown to be secreted from skeletal muscle during exercise and has been suggested to signal to the liver. Therefore, the aim of this study was to investigate the role of skeletal muscle IL-6 on hepatic glucose regulation and substrate choice during prolonged exercise. Skeletal muscle-specific IL-6 knockout (IL-6 MKO) mice (age, 12-14 wk) and littermate lox/lox (Control) mice were either rested (Rest) or completed a single bout of exercise for 10, 60, or 120 min, and the liver was quickly obtained. Hepatic IL-6 mRNA was higher at 60 min of exercise, and hepatic signal transducer and activator of transcription 3 was higher at 120 min of exercise than at rest in both genotypes. Hepatic glycogen was higher in IL-6 MKO mice than control mice at rest, but decreased similarly during exercise in the two genotypes, and hepatic glucose content was lower in IL-6 MKO than control mice at 120 min of exercise. Hepatic phosphoenolpyruvate carboxykinase mRNA and protein increased in both genotypes at 120 min of exercise, whereas hepatic glucose 6 phosphatase protein remained unchanged. Furthermore, IL-6 MKO mice had higher hepatic pyruvate dehydrogenase (PDH)Ser232 and PDHSer300 phosphorylation than control mice at rest. In conclusion, hepatic gluconeogenic capacity in mice is increased during prolonged exercise independent of muscle IL-6. Furthermore, skeletal muscle IL-6 influences hepatic substrate regulation at rest and hepatic glucose metabolism during prolonged exercise, seemingly independent of IL-6 signaling in the liver.

General information
State: Published
Organisations: University of Copenhagen
Authors: Bertholdt, L. (Ekstern), Gudiksen, A. (Ekstern), Schwartz, C. V. L. (Intern), Knudsen, J. G. (Ekstern), Pilegaard, H. (Ekstern)
Pages: R626-R636
Publication date: 7 Apr 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: American Journal of Physiology - Regulatory Integrative and Comparative Physiology
Volume: 312
Issue number: 4
ISSN (Print): 0363-6119
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.03 SJR 1.462 SNIP 0.993
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.68 SNIP 1.017 CiteScore 3.11
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.721 SNIP 1.154 CiteScore 3.35
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.768 SNIP 1.258 CiteScore 3.73
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.645 SNIP 1.209 CiteScore 3.58
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.535 SNIP 1.165 CiteScore 3.34
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.522 SNIP 1.134
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.498 SNIP 1.063
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.604 SNIP 1.066