Abstract

Hypothermia is a key symptom of sepsis, but the mechanism(s) leading to hypothermia during sepsis is largely unknown and thus no effective therapy is available for hypothermia. Therefore, it is important to investigate the mechanism and develop effective therapeutic methods. Lipopolysaccharide (LPS)-induced hypothermia accompanied by excess nitric oxide (NO) production leads to a reduction in energy production in wild-type mice. However, mice lacking inducible nitric oxide synthase did not suffer from LPS-induced hypothermia, suggesting that hypothermia is associated with excess NO production during sepsis. This observation is supported by the treatment of wild-type mice with α-lipoic acid (LA) in that it effectively attenuates LPS-induced hypothermia with decreased NO production. We also found that LA partially restored ATP production, and activities of the mitochondrial enzymes involved in energy metabolism, which were inhibited during sepsis. These data suggest that hypothermia is related to mitochondrial dysfunction, which is probably compromised by excess NO production and that LA administration attenuates hypothermia mainly by protecting mitochondrial enzymes from NO damage.