

P-617

Role of changes in cardiac metabolism following endotoxemia-induced cardiac dysfunction

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Background and Objective: To determine whether drug-induced alterations in cardiac metabolism may be a viable strategy to reduce endotoxemia-mediated cardiac dysfunction, we assessed endotoxemia-induced changes in glucose and fatty acid metabolism. **Materials and Methods:** Endotoxemia was induced in male Sprague-Dawley rats by lipopolysaccharide (4 mg/kg, i.p.) 6 hrs prior to heart removal for ex vivo assessment of left ventricular (LV) work and rates of glucose metabolism (glucose uptake, glycogen synthesis, glycolysis and glucose oxidation) and palmitate oxidation. **Results:** Endotoxemic hearts had impaired LV function as judged by echocardiography in vivo (% ejection fraction, 66.0 ± 3.2 vs 78.0 ± 2.1 , $p<0.05$) or by LV work ex vivo (2.14 ± 0.16 vs 3.28 ± 0.16 , Joules.min⁻¹.g dry wt⁻¹, $p<0.05$). However, rates of glucose uptake, glycogen synthesis, glycolysis, and glucose oxidation were not altered. Palmitate oxidation was lower in endotoxemic hearts in proportion to the decreased workload, thus metabolic efficiency was unaffected. In hearts reperfused following global ischemia, untreated hearts had impaired recovery of LV work (52.3±9.4%) whereas endotoxemic hearts had significantly higher recovery (105.6±11.3%, $p<0.05$). During reperfusion, fatty acid oxidation, acetyl CoA production and metabolic efficiency were similar in both groups. **Conclusion:** As impaired cardiac function appeared unrelated to depression of energy substrate oxidation, it is unlikely that drug-induced acceleration of fatty acid oxidation will improve mechanical function. The beneficial repartitioning of glucose metabolism in reperfused endotoxemic hearts may contribute to the cardioprotected phenotype.

Key Words: Endotoxemia, cardiac function, glucose metabolism, palmitate metabolism

P-618

The effect of nobiletin on inflammatory response, oxidative stress, and apoptosis in a model of Parkinson's disease induced by intranigral injection of lipopolysaccharide in the rat

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Background and Objective: Nobiletin is a flavonoid in citrus. The antioxidant, anti-inflammatory and anti-apoptotic properties of nobiletin have been observed. The aim of the present study was to investigate the effect of nobiletin (NOB) on inflammatory response, oxidative stress and apoptosis in an experimental model of Parkinson's disease (PD) induced by intranigral injection of lipopolysaccharide (LPS) in rats.

Materials and Methods: Male rats ($n = 28$) were divided into four groups: sham, sham under treatment of NOB, lesion and lesion treated with NOB. To achieve unilateral lesion of the nigrostriatal system, rats received 5 µg of LPS into the right substantia nigra. NOB was administered p.o. at a dose of 10 mg/kg/day from one hour after surgery till one week later. One week post-surgery, oxidative stress markers, inflammatory factors, and severity of apoptosis were measured.

Results: The results showed that treatment with NOB significantly decreased malondialdehyde (MDA), reactive oxygen species (ROS), increased glutathione (GSH), superoxide dismutase (SOD) activity, decreased inflammatory factors including nuclear factor-kappa, Toll-like receptor 4, tumor necrosis factor and also decreased DNA fragmentation in LPS group.

Conclusion: Administration of NOB to LPS-induced PD reduces oxidative stress, inflammation and apoptosis, which may potentially be of benefit for ancillary therapy of PD.

Keywords: Nobiletin, Oxidative stress, Inflammation, Apoptosis, Parkinson's disease, Lipopolysaccharide