Single bout of endurance exercise increases NNMT activity in the liver and MNA concentration in plasma; the role of IL-6

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Abstract:
Background: Methylnicotinamide (MNA) displays vasoprotective activity, however, the regulation of the activity of nicotinamide-N-methyltransferase (NNMT), is largely unknown. We analyze a possible involvement of IL-6 in the activation of NNMT-MNA pathway during an endurance exercise.

Methods: FVB, C57Bl/6J IL6+/− and C57Bl/6J IL-6−/− mice were subjected to the single bout of endurance exercise consisting of 90 min of swimming. Thereafter, exercise-induced changes in NNMT activity in the liver as well as concomitant changes in the concentration of MNA and its further metabolites in plasma were analyzed.

Results: In two strains of mice (FVB and C57Bl/6J IL6+/−) 90 min of swimming resulted in approximately 2–3 folds increase in NNMT activity (from 0.14 ± 0.03 to 0.421 ± 0.02 pmol/min/mg, p < 0.05 and from 0.2 ± 0.06 to 0.35 ± 0.07 pmol/min/mg, p < 0.01, respectively) and concomitant increase in the plasma concentration of MNA (from 157 ± 15.06 to 230 ± 16.2 ng/ml, p < 0.01, and from 77.05 ± 14.6 ng/ml to 152.55 ± 58.4 ng/ml; p < 0.01, respectively). However, in C57Bl/6J IL-6−/− mice 90 min of swimming did not change liver NNMT activity (from 0.25 ± 0.07 to 0.23 ± 0.06 pmol/min/mg), while MNA concentration in plasma rose approximately two-fold (from 65.3 ± 30.9 ng/ml to 124.8 ± 58.8 ng/ml; p < 0.05).

Conclusions: We demonstrated for the first time that NNMT–MNA pathway is activated by a single bout of endurance exercise. Interestingly, exercise-induced activation of NNMT in the liver involves IL-6, while the rise in MNA concentration in plasma was partially IL-6-independent. Taking into the consideration the pharmacological activity of MNA, IL-6-dependent and IL-6-independent activation of NNMT, may contribute to the exercise capacity. The physiological role of NNMT in the exercise warrant further studies.

Key words: endurance exercise, interleukin-6, nicotinamide N-methyltransferase, 1-methylnicotinamide