Catecholamines enhancement of iNOS-induced NO biosynthesis involves CAT-1 and CAT-2A

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摘要

Abstract

Catecholamines enhance inducible nitric oxide synthase (iNOS) expression that results in nitric oxide (NO) overproduction in lipopolysaccharide (LPS)-stimulated macrophages. L-arginine transport mediated by cationic amino acid transporters (including CAT-1, CAT-2, CAT-2A, and CAT-2B) is crucial in regulating iNOS activity. We sought to assess the effects of catecholamines on L-arginine transport and CAT isozyme expression in stimulated macrophages. Confluent RAW264.7 cells were cultured with LPS with or without catecholamines (epinephrine or norepinephrine, 5 × 10−6 M) for 18 h. NO production, L-arginine transport, and enzyme expression were determined. Our data revealed that LPS co-induced iNOS, CAT-2, and CAT-2B expression, whereas CAT-1 and CAT-2A expression remained unaffected. Significant increases in NO production and L-arginine transport (approximately eight-fold and three-fold increases, respectively) were found in activated macrophages. Catecholamines significantly enhanced NO production and L-arginine transport (approximately 30% and 20% increases, respectively) in activated macrophages. Catecholamines also enhanced the expression of iNOS, CAT-1, and CAT-2A but not CAT-2 or CAT-2B in LPS-stimulated macrophages. Furthermore, the enhancement effects of catecholamines were inhibited by either dexamethasone or propranolol. We provide the first evidence to indicate that L-arginine transport in activated macrophages could be enhanced by catecholamines. Furthermore, this catecholamine-enhanced L-arginine transport might involve CAT-1 and CAT-2A but not CAT-2 or CAT-2B.