NG\textsuperscript{4}-NITRO-L-ARGININE AND ITS METHYL ESTER INHIBIT BRAIN SYNTHESIS OF KYNURENIC ACID POSSIBLY VIA NITRIC OXIDE-INDEPENDENT MECHANISM

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The effect of nitric oxide synthase (NOS) inhibitors on the brain production of endogenous glutamate receptor antagonist, kynurenic acid, was estimated \textit{in vitro}. Under standard incubation conditions NG\textsuperscript{4}-nitro-L-arginine, but not NG\textsuperscript{6}-nitro-L-arginine methyl ester, up to 5 mM, or 7-nitroindazole, up to 100 \textmu{}M, inhibited \textit{de novo} synthesis of kynurenic acid in cortical slices. However, during prolonged incubation, NG\textsuperscript{4}-nitro-L-arginine methyl ester also reduced the production of kynurenic acid. The substrate for NOS, L-arginine (up to 5 mM), did not influence kynurenic acid synthesis and did not reverse the NG\textsuperscript{4}-nitro-L-arginine-evoked changes, suggesting that the observed effects are not related to disturbed generation of NO. Enzymatic studies revealed that NG\textsuperscript{4}-nitro-L-arginine and its methyl ester blocked the activity of brain kynurenine aminotransferase (KAT) I. The activity of KAT II was diminished only by NG\textsuperscript{6}-nitro-L-arginine. Kinetic analyses have shown that NG\textsuperscript{3}-nitro-L-arginine and its methyl ester reduce $V_{\text{max}}$ and increase $K_{m}$ of KAT I, whereas NG\textsuperscript{6}-nitro-L-arginine diminishes $V_{\text{max}}$ of KAT II. In conclusion, we report that NG\textsuperscript{4}-nitro-L-arginine and its methyl ester impair brain synthesis of kynurenic acid, probably via NO-independent mechanism, which could contribute, at least partially, to the enhancement of neurotoxicity or seizures observed in some experimental designs based on their use.

\textbf{Key words:} brain, kynurenic acid, kynurenine aminotransferases, nitric oxide, NG\textsuperscript{4}-nitro-L-arginine, NG\textsuperscript{6}-nitro-L-arginine methyl ester, \textit{in vitro}

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