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The Role of Adrenoreceptors in the Regulation of EROD Enzymatic Activity

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The aim of this study was to investigate the effect of adrenergic receptors in the regulation of ethoxyresorufin 7-dealkylase (EROD) enzymatic activity, which is catalyzed by CYP1A1. This cytochrome is involved, among others, in the metabolism of polycyclic aromatic hydrocarbons. Basal and B[α]P-induced EROD activity was determined fluorometrically in liver microsomes of adult male rats. Reserpine was used for central and peripheral catecholamine depletion and guanethidine for peripheral sympathectomy. In addition, a variety of adrenergic agonists and antagonists were used in order to test the hypothesis that adrenergic receptors are involved in the regulation of CYP1A1 (phenylephrine: α1-agonist; prazocin: α1-antagonist; dexmedetomidine: α2-agonist; atipamezole: α2-antagonist; isoprenaline: β1/β2-agonist and propranolol: β1/β2-antagonist). The data revealed that: 1) The sympathetic nervous system (SNS) plays a significant role in the regulation of CYP1A1, mainly via α1 and/or β2-adrenoreceptors. Blocking of these receptors, predominantly on the hepatic cell membrane, markedly suppressed EROD activity. 2) On the other hand, it seems that the central nervous system (CNS) plays a central role in the regulation of EROD inducibility by B[α]P, since reserpine administration strengthened this induction, while guanethidine had no effect. In particular, blocking of α1 adrenergic receptors with prazocin enhanced EROD inducibility by B[α]P and blocking of β2-receptors with propranolol diminished it. Blocking of α2-adrenoreceptors with atipamezole resulted in an increase of this induction. In conclusion, the findings suggest that the regulation of basal EROD activity is under control of the SNS, while the CNS is involved in the regulation of EROD inducibility by B[α]P.